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WASHINGTON UNIVERSITY MEDICAL ALUMNI QUARTERLY

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  - *Charles Huggins, M.D., D.Sc.*
  - *Edwards A. Park, M.D., D.Sc.*
  - *Philip A. Shaffer, Ph.D.*
  - *Robert J. Terry, M.D.*
- Proceedings of Washington University Medical Society

Vol. XIII APRIL, 1950 No. 3

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The Washington University
Medical Alumni Quarterly

VOL. XIII APRIL, 1950 NO. 3

50th Anniversary of Medical School Celebrated on February 21

Centennial of Robert S. Brookings' Birth also Noted

More than 700 persons attended the dinner at the Chase Hotel in St. Louis on February 21 which climaxed activities celebrating the 50th Anniversary of the School of Medicine and the centennial of Robert S. Brookings' birth.

Main speaker for the evening was Dr. Alan Gregg, director of the Division of Medical Sciences of the Rockefeller Foundation, whose topic was, "Time and the University." Other speakers were Dr. Philip A. Shaffer, former dean of the School of Medicine; Dr. Robert J. Terry '95, professor emeritus of anatomy; Dr. Robert A. Moore, Dean; and Mr. Harry Brookings Wallace, president of the Corporation. Chancellor Arthur H. Compton presided.

The cornerstone for the new Cancer Research Building was laid at 2:00 P. M. by Mr. Wallace. Dr. Leonard Scheele, surgeon-general of the U. S. Public Health Service, spoke briefly of the close cooperation between the School and that organization. Among the special guests were Mrs. Robert S. Brookings of Washington, D. C., and Dr. J. R. Heller, Jr., chief of the National Cancer Institute in Bethseda, Md.

At a special convocation in Graham Chapel that morning, honorary degrees were conferred upon Dr. Abraham Flexner, whose criticism of the medical school aroused Robert Brookings' interest in reorganizing it in 1910; Dr. Ernest W. Goodpasture, professor of pathology and dean, Vanderbilt University Medical School; Dr. Charles B. Huggins, professor of surgery, University of Chicago; and Dr. Edwards A. Park, professor emeritus of pediatrics, John Hopkins University School of Medicine. Dr. Harold G. Moulton, president of the Brookings Institution in Washington, D. C., gave the address on *Robert Somers Brookings.*

Guests at the dinner received souvenir booklets telling the history and development of the School of Medicine, copies of which have been mailed to all medical alumni, along with the text of Dr. Gregg's address.

The talks by Dr. Shaffer and Dr. Terry and the scientific papers presented during the afternoon program by Drs. Goodpasture, Huggins and Park are printed on the following pages of this issue.

Some Aspects of Twentieth Century Research on Infectious Diseases

by Ernest W. Goodpasture, M.D., D.Sc.

Professor of Pathology, Vanderbilt University School of Medicine, Nashville, Tennessee

For a student of medicine I can think of no better fortune than to have labored in this field of his choice within the past fifty years. Notwithstanding the fact that the preceding half century was surcharged with the energy of unprecedented scientific discoveries, and that among these were the very fundamentals for medical progress, the acceptance and incorporation of the results into a widely available general medical education was largely reserved for the twentieth century. The excitement to the pursuit of adventure in scientific inquiry generally, but especially in the study of infectious disease, culminated in such an acceleration of discovery in the latter years of the last century that established institutions for teaching and training were quite inadequate to the task of assimilating, much less propagating, the new knowledge. This was certainly the case generally with schools for medical education. The fact that the then recently-organized Medical School of Washington University demonstrated the inherent strength and soundness not only to survive the hectic days of reform during the first decades, but to assume in face of the challenge a distinguished position of leadership in the new era of medicine, are accomplishments which we are most fortunate and privileged to commemorate and to honor today.

I wish to speak primarily about research and the science of infectious diseases rather than of medical education, although the performance and the fruits of research are for medicine the life blood of teaching and practice. In the field of research as well as of teaching, Washington University School of Medicine has played a most distinguished role and much that I shall have to say about infections will simply be coals brought to Newcastle, for the work of C o w d r y, Bronfenbrenner, Margaret Smith, their collaborators and colleagues have enriched many aspects of knowledge of this subject.

Fifty years is a brief period in history computed by time, but measured in terms of the crowding of significant scientific accomplishments, the first half of this wonderful and awful century has been for medicine, and I believe for human affairs generally, the longest era in the eventful life of mankind.

It would be difficult to exaggerate the change in circumstances and outlook of people, especially in our own country, that has come to pass in the present century with respect to infectious diseases. Despite its relative rapidity this change has been so logical and acceptable that we are hardly aware of it.

Although most of the great epidemics have ceased their recurrent disasters, it was only about the time Eliot Sem-

inary, the forefather of Washington University, was founded that according to Geddes Smith the United States suffered one of its periodic outbreaks of cholera. St. Louis was visited by such an epidemic that, when the City authorities faltered, a voluntary committee not only cleaned up the town and burned tar and sulphur but, for good measure, had bonfires lighted in the streets—without, however, preventing the death of 4,568 people. We do not fear cholera now, nor smallpox, diphtheria, meningitis, yellow fever, nor plague and typhoid fever as our forefathers did.

Your present medical students born about 1930 could at birth look forward to a life of health and activity totaling on the average about 60 years, although their fathers born around 1900 belong to a group who could expect only about 47 years, while their grandsires, who might have been as old as Washington University, could anticipate at birth a longevity of approximately a ten year briefer span. These impressive changes have come about, largely since the turn of the century, through the establishment and development of a number of scientific activities dependent upon the bacteriological era, such as sanitary science and engineering, the science of immunology and its practical copartner preventive medicine, the science and art of chemo-therapy, rationally begun by Paul Ehrlich, and through concurrent improvements in the art of medicine. These activities are providing some of the twentieth century luxuries that emanated from basic research in the field of infectious diseases before this century began.

Contemporary reliefs and present requirements of civilized life provided for populations by preventive medicine and public health are so thoroughly accepted that they no longer excite passing wonder or praise. But to contemplate a surgical operation, an attack of pneumonia or tularemia or even a bout with tuberculosis (recently demoted from second to sixth place or lower among mankillers), with the relative equanimity now possible, is to acknowledge an achievement of medical care and modern therapy for the individual that is still of exciting interest. The twentieth century is indeed the prime beneficiary of the preceding one, at least in medicine; nevertheless it has assumed with vigor its own responsibility for carrying the torch of research while it has sought to assimilate the knowledge transmitted to it from the past.

Although our century is only half-spent we can already reflect upon the facts that for bacteriology the Chaos of Linnaeus has been transformed into the 6th edition of Bergey's Manual; the empirical success of Jenner has evolved into the practical as well as the esoteric science of immunology; a therapeutic nihilism has succumbed to a sulfa- and antibiotic-happy general practitioner; the *contagium vivum fluidum* of Beijerinck is now represented by a varied assortment of photographic images of particulate viruses revealed by the electron microscope, quite unknown to our forefathers.

Both the practical achievements and the basic insights of our time have been the true descendants of the great stress

upon fundamentals that shortly preceded them, and I wish to devote the time allotted me to a brief consideration of what I regard as expressions of contemporary assault upon the same old fundamentals in new dress, as exemplified by certain aspects of research in the field of infectious diseases. Permit me in the first place to indulge a passing reflection upon a current technique for supporting scientific inquiry, including that concerned with infections, as it relates to provision for such basic, as contrasted with developmental, research.

In considering the research of the past half century, especial emphasis must be placed upon the contributions to knowledge, to understanding and to utility that finally resulted from the long and difficult groping for refinement of the intellectual cast of age-old biological problems, and from the patient search for ways and means of elucidating them. The nineteenth century was particularly distinguished by a culmination of this pursuit in a degree of success, along many scientific fronts, such as the intellect of man had never before achieved, and, in breadth of significance, is not likely to experience in a similar period of time.

The twentieth century has thus far been notably characterized by the fruitful development of applicable knowledge implicit in the major discoveries and interpretations of a more fundamental nature. Our half century, however, has not concerned itself alone with developmental research, as significant as that has been. It has in addition and in its own manner, with new tools and new concepts, hewn away at the old problems, which always persist, despite strategic conquests of understanding, because they can never be completely solved by the scientific method. The important question nevertheless confronts the support of science today as to whether the brilliance and impressiveness of developmental efforts have not so overshadowed the less spectacular pursuit of basic understanding, particularly of biological phenomena, that adequate emphasis upon the provision for the latter has become seriously lacking. This problem derives a particular significance from the fact that neglect of the long term view involves a corresponding relaxation in the effort to provide an environment that is appealing and satisfying for the careers of investigators who are primarily scholars and teachers and upon whom rests eventually the inspiration to research, whether designed for inventions and developments or otherwise. A proper environment must offer great freedom to follow parts of learning that only the curiosity and intuition of the inquirer dictate; and this can for the most part be best maintained within the university, provided reasonable financial resources to assure continuity are available.

One hears a great deal today about basic or fundamental research and science. What is really meant by this distinction is a definition of attitudes of investigators and of the problems they undertake to solve. The procedure of research is much the same irrespective of purpose or problem, but the attitudes of investigators differ. The

underlying psychological differential factor, I believe, is the factor of utility, and if I interpret it correctly, American science has been thus far predominantly utilitarian. Such an emphasis was certainly enhanced by conditions imposed by war. I do not intend in the least to disparage the utilitarian motive of research. Certainly in medicine the benefits that have accrued from this approach to problems have been of inestimable humanitarian value, especially for the prevention and treatment of infectious diseases. In some fields of science perhaps one might cogently question the predominant directions to which utilitarian motives have pointed scientific research, but not in medicine. Medicine is an acceptable humanitarian art; the art of war must occupy a different category.

Although, because of its immediately obvious significance, the utilitarian approach to science is the more readily understood and supported, it should be of much concern to all whether or not adequate provision is made for the pursuit of science under the impetus of another motivation; namely, the exercise of a free and fertile intellectual curiosity whose ultimate aim is a better understanding of life and its environment. One of the possible drawbacks to a predominantly utilitarian approach is its inevitable accompaniment of tension, pressure and hurry. It is as though all needs must be served at once and that preemience of one sort or another must be maintained. It is somewhat of an ironical twist that justification of basic research should need be founded upon the manifest dependence of development and utility upon the primarily non-utilitarian, transcendent, free inquiries to satisfy curiosity and to fortify understanding.

The pursuit of knowledge to enrich understanding need not be hurried; it cannot be measured in time because it has no end; it is a perpetual and eternal pursuit; therefore, it can be approached with composure, dignity and respect. It would seem most unfortunate that such an approach to science should ever become completely dependent upon or inextricably involved with the temporary grant-in-aid procedure for a "project." A project is an entity; it is something concrete; it can be described, defined, budgeted and evaluated by a remote committee; it can be time-limited to a year or so; it has the crispness of a contractual relation, a *quid pro quo;* it has the fiscal address of a good business proposition; it has a financial appeal and it gets a grant-in-aid. The pursuit of science, however, must go on beyond a project, beyond an era of development. It should continue, I believe, in our institutions of learning, the universities, and they should be supported for the long pull, not merely for the short haul, if basic research is to flourish.

While my chief concern will be with some basic aspects of investigations of infectious diseases, and then only within limited areas, we are all aware that it takes a concatenation of events of apparently wide diversity to inflict so overwhelming an impact upon human affairs as the achievements of science have wrought within the memory and experiences of living men. Wealth and

war as well as wonderment have contributed to the total picture, and bewilderment and fear have been the partners of hope in the aggregate effect. One result however has been the increasing availability to medical problems of the underlying sciences with their special knowledge and methods. Mathematics, physics, chemistry and biology all contribute now to the armamentarium of research related to infection.

Where do the fundamentals lie now in the melee of developmental, exploitative and basic research in the field of infectious diseases in our century? Wherever they are to be found it is certain that America must assume its long-delayed responsibility for recognizing them, and providing for their proper and unending cultivation.

The problems that it was the magnificent fortune of the nineteenth century to solve, with a degree of accuracy sufficient to establish on secure foundations so many fundamental sciences, had matured and sharpened in outline through the preceding centuries of all human experience. They culminated in a splendid outburst of illuminating knowledge, the more spectacular by virtue of eminently useful potentialities. It is of particular significance to the field of infectious diseases that this culmination came about not only with the ripening of theoretical speculations but with the invention of tools and methods that could be suitably applied to their solution, and more specifically, with the emergence of two truly remarkable men, Louis Pasteur and Robert Koch. The convergence of these factors sooner or later was inevitable. It must be remembered, however, that the enlightenment that resulted was, like all scientific knowledge, a relative progress, not an elimination of the basic problems. These remain and with each advance in applicable technical facilities there will always be a research and a refinement of the ancient and perpetual problems of life processes.

The great and memorable epoch in the history of infectious disease reached in the last decades of the nineteenth century was such as perhaps the world will not witness again. A dramatic moment in this epoch which epitomizes for me much that had gone on before, and accentuates a fateful turning point, is that described by Dr. Bulloch in his commendable history of bacteriology. Part of the episode at least was recounted to him by Lord Lister. The occasion was the International Medical Congress at London in 1881. Gathered together in the Physiological Laboratory of Kings College were a group of eminent figures of the time. Standing side by side were Pasteur, Lister and Koch. Burdon-Sanderson and Chauveau were with them and the incorrigible Charlton Bastian. Pasteur had not met Koch before but when he saw his demonstration of bacterial cultures on solid media he turned to him to exclaim, "It is a great advance, Monsieur." Bastian, the English heterogenist, who in spite of Pasteur's exquisite experiments and eloquent expositions could not be budged from his belief in spontaneous generation, was expounding his old views with renewed ardor. Unable to contain himself Pasteur threw up his

hands and cried in tones of utter consternation and repugnance, "My God, my God, do you still believe that? My God, it just can't be possible!" The old doctrine of spontaneous generation was a dead duck it seemed, and Pasteur gave it a parting kick. Koch's new techniques for bacterial culture lay before them. These assured a rich fruition for the new doctrine of specific microbial etiology of infectious disease then born.

The impetuous flow of the hot lava of knowledge welling from the bacteriological volcanoes rolled on mightily and when it lapped upon a resistant terrain it swirled and swept around it, speeding on to create the two great streams of bacteriology and immunology which in its wake hardened into the firm foundations of these two new sciences. But the *terra incognita* left behind, and relegated to the "mopping up" operations of the twentieth century, proved to be a vast terrain of rich potentialities for those who went in. It was the Lilliputian land of the viruses, the rickettsiae and sundry recalcitrant obligate and faculative intracellular parasites that the methods of Pasteur and Koch had failed to dislodge.

The fact should not be minimized that both Jenner and Pasteur confronted the inscrutable smallpox and rabies and wrested from them practical values and basic concepts that went into the structure of immunology. Furthermore Iwanowski and later Beijerinck, with the bacteria-withholding filters they devised, had already made the fundamental discovery of the active agent of tobacco mosaic, the first "filterable" virus; and as the century closed Loeffler and Frosch reported the filterability of the virus of foot and mouth disease, the first "filterable" virus discovered in an infectious disease of animals. It should be an admonition too that, had more attention been paid to the nearly contemporary filtration of the agent of yellow fever accomplished by Walter Reed and his associates in Cuba, much valuable time might have been saved and subsequent errors avoided. Nevertheless a broad field for exploitation remained in this by-passed continent of infectious diseases, and it has been one of the major undertakings of twentieth century scientists to explore its secrets.

In confining myself to the subject of viruses I have no intention of minimizing the importance of both developmental and basic research along many other lines within the general province of the infectious disease. One could not pretend briefly to estimate the extent of advancement of bacteriology with its many theoretical and practical attainments, nor of immunology, the new science that so uniquely unites in the study of infectious disease the basic disciplines of mathematics, chemistry, physics and physiology. One competent to do so could, and much more interestingly, tell of the newer developments and theoretical implications of the antibiotics whose exciting effects and potentialities astound us daily.

My greater, though limited, familiarity with the viruses is my excuse for using them to illustrate particularly a type of basic problem, derived from a group of infectious diseases, which has little immediate promise of utility

and may never have, although this problem possesses in my opinion the fundamental character of those upon which the founders of bacteriology were forced to prevail in order to advance understanding and to refine theory.

The pathogenic microorganisms with which the early bacteriologists dealt successfully were those possessed of such independence of function that they could readily be cultivated in or upon suitable non-living media, and, when infecting a living host, they utilized in general its extracellular nutritive fluids for their reproductive needs. This was not the case with the viruses and the rickettsiae, nor with some bacterial and protozoal forms which at least in certain stages of their existence inhabit the interior of cells of their host.

All the evidence we have accumulated with respect to viruses is indicative of their requirement of an intracellular environment and of the supportive contributions from the living infected cell itself for their persistence and multiplication. It was this fact which defeated the early bacteriologists and has presented unique problems to the investigators of our own times.

Because of the peculiar relationship of viruses with cells, I cannot refrain at this point from paying tribute, in part at least as a pathologist, to the great group of biologists in a broad sense who, immediately preceding the bacteriologists of the last century, placed on a firm foundation the great cellular theory. I refer especially to the botanist Matthias Schleiden and his copartner in animal cytology, Theodore Schwann. Even more significant for biology, and the eventual study of infectious diseases, was the influence of the eminent pathologist Rudolph Virchow, who made through cytology and cellular pathology a contribution to the struggle against the doctrine of spontaneous generation similar to that which Pasteur made for microbiology. The dictum of Virchow "*omnis cellula e cellula*" marked the death of the doctrine of heterogenesis, represented by the blastema theory of Schleiden and of Schwann, as applied to the cells of animal tissues. The establishment of the cellular theory of animate structure was perhaps the greatest contribution to biology and to medicine of all time.

The identification and classification of cells in complex organisms has played an important role in the study and understanding of the virus diseases. The significance of the relationships that exist between obligate intracellular infective agents and the cells they inhabit has hardly begun to be explored, although in those relationships lie some of the most fundamental phenomena of biology.

The cellular manifestations of virus activity ultimately underlie all research with these agents, because no device has succeeded in causing them to multiply in the absence of living susceptible cells. Consequently all viruses that are known are pathogenic agents and their activity can be demonstrated only by the results of infection. The cellular manifestations of virus activity have been guides to the discovery, identification and pathogenesis of many viral infections. By their study alone experimental demonstration has been made

of the intracellular location of viruses, such as that of fowl-pox. Chemical and physical researches utilizing a group of plant viruses, while of the greatest significance, are ultimately controlled by and concerned with the biological interaction between the agent and the cell it affects.

There are three relatively gross cellular evidences of virus activity which have been helpful in the identification of infection. These are hyperplasia, the formation of intracellular "inclusions," and necrosis, which probably always precedes the manifestation of inflamation. Conversely the effects of host cells upon viruses are notably multiplication of virus particles and, under suitable conditions, certain irreversible changes or mutations of them.

Lending themselves to a determination of the specificity of a given virus infection were various immunological methods which largely developed from similar methods elaborated in the study of bacterial diseases. Such methods are those of complement fixation, agglutination and precipitation. But it was found that another effect not commonly encountered in immune serum from bacterial infections, namely an inactivating effect, was frequently demonstrable. These methods proved of great use in diagnosis of specific viral infections and in the determination of antigenic differences in strains of the same virus, although the use of immune serum as a therapeutic or preventive measure has been generally disappointing. The application of the methods of immunology have also importantly enhanced the success of efforts to purify viruses.

Because of their recondite nature, the "purification" of viruses is a desideratum of the highest order for their further study; and while the application of all the methods that physical, chemical and biological research made available to investigators from time to time has been as yet rarely successful in this attempt, it has served to give a much clearer idea of their structure. An exceptional success, however, has attended attempts initiated by Stanley to purify mosaic viruses of plants. Beijerinck, as I have mentioned, spoke of a *contagium vivum fluidum* in reference to the virus of mosaic disease of tobacco, and the chemical and physical research of Stanley has succeeded in identifying the virus with a large, crystallizable, nucleo-protein molecule. Research with other viruses has revealed a very variable and often complex structure of the particles of most of them. Although only a begining of chemical analysis has been made, physical determinations of size and shape have shown a very wide range, overlapping with bacteria at one end and with protein molecules at the other.

The two great basic problems presented by the study of viruses are their structure and their biological significance. A good indication of the present elementary state of understanding of viruses are two contrasting theories of their nature. The one, originated by the late Dr. Robert Green, is to the effect that they represent retrograde evolutionary forms of probably extinct, but originally free-living, microorganisms. The other, emerging from the work of Stanley, although not yet generalized, is

that a virus can be a large molecule of nucleoprotein primarily derived from the cells of hosts. Stanley's work has been concerned rather with the mechanism of reproduction of uni-molecular viruses than with conjectures as to their origin.

In view of these speculative points of view (and speculation is bound to be of importance to future work and interpretation of factual data), it is of interest to consider closely the biological significance of viruses. Whether they are all living entities is a question that involves a definition of life, and is not of immediate relevance. Becaus viruses vary in size and complexity, ranging from larger ones which overlap with known bacteria to minute ones whose structural characteristics are those of a chemical molecule, there are two opposed starting points for speculation as to their origin and biological significance. The facts, however, have demonstrated attributes of viruses, even those of unimolecular structure, which differentiate them from any other chemical molecules. These attributes are their capacity for reproduction, even in unaccustomed hosts though only within special living cells, and their ability to mutate. These are characteristics possessed by living beings although evidence of metabolism is still lacking. Thus whether one begins his speculation at the bacterial pole of the problem or at the molecular level, his starting point assumes the existence of a particle having at least some of the important qualities of free-living biological entities, not known to be possessed by other protein molecules.

Green's hypothesis is the concept of a retrograde evolutionary change from a free-living microbial form. Through parasitism in another living cell, the microorganism gradually loses its independent functions. One activity after another ceases as each becomes successively supplied by the parasitized cell until through reduction in complexity and substance is eventually reaches the simplicity of a single molecule. The facts we possess do not permit at present a logical pursuit of this hypothesis to the vanishing point of the supposed degraded bacterium. Factual reasoning therefore stops with a molecule still possessed of the properties of reproduction and mutation. This is the hypothesis that at present seems to be most persuasive. It has the very great advantage that it begins with an entity, a bacterium, endowed with the attributes of life. Starting at the other end of the problem, at the molecule level, speculation concerning the origin of a virus comes, as Rivers has suggested, very close to the old problem of spontaneous generation that Pasteur thought he had kicked down stairs for good. Such an hypothesis would assume that in some unknown manner the substance of the living protoplasm of a cell can give rise to a nucleo-protein molecule of large size which acquires during its formation and development the ability to bring about its own reproduction and the ability to mutate under certain circumstances. Bearing upon this problem is the recently published work of Wildman, Cheo and Bonner in which evidence is presented that tobacco mosaic virus nucleo protein is synthesized in

leaf cells at the expense of the normal nucleoprotein found in the cytoplasm of these cells.

From the standpoint of biological speculation the possibility of an origin of a virus molecule *de novo* from protoplasm would seem to me to be the more intriguing because it would represent an evolutionary rather than a retrocessive phenomenon. Reason alone would tell us science sooner or later must grapple with this problem, and now we have it presented in a way that experiment can approach it.

The two views of origin of unimolecular viruses are not mutually exclusive, but the factual basis of either, according to present knowledge, is the existence of a single molecule possessed of the attributes of reproduction and mutation, in other words possessed of certain important characteristics of living things. The fact that molecular viruses can mutate is evidence of their liability and, in fact, of their adaptability. It is of very great importance in this connection that Knight has shown definite differences in the amino-acid content of certain mutant strains of tobacco mosaic virus. According to Stanley, "These results indicate that the mutation of a virus can be accompanied by a change in the concentration of one or more amino-acids in the virus structure, by the introduction of one or more new amino-acids into the virus structure, or by the elmination of an amino-acid from the virus structure." Stanley presumes that changes of this type are also responsible for alteration of genes.

With reference to mutation of viruses, students of bacterial viruses or bacteriophages, the agents that parasitize bacterial cells, speak with confidence of genes and the genetic structure of these agents.

According to a recent review by Dr. Bronfenbrenner, a leader of long standing in this general field, knowledge of genetic mechanisms in bacterial viruses is growing rapidly, owing partly to the application of rigorous genetic methods by Hershey and others and partly to the use of techniques developed for the study of viral growth and interactions by Delbruck and Bailey. The genetic pattern of certain viruses at least has been found to be far more complex than had been suspected. For example, it is calculated on the basis of recent experiments of Lura that one strain of a virus infectious for *Escherichia coli* (T_2) contains a minimum of about 20 genes.

The bacterial viruses have proved to be a very interesting group. Some of them are possessed of a tail and have a tadpole shape, as seen in electron micrographs, and exhibit a differentiated internal structure. The T_2 strain, possessing a calculated minimum of about 20 genes, is one of the larger of this group, measuring 60 to 80 mu in diameter, which is only about six times the diameter of the smallest virus, that of foot and mouth disease. On chemical analysis of preparations of T_2 strain of coli bacteriophage, Hook and his coworkers found that the virus weighs about 10^{-15} Gm. per infectious unit. The material was composed chiefly of protein, but with desoxyribonucleic acid in the high proportions of 40%. Kalmanson and Bronfenbrenner have found

only a small amount of phosphorus in a closely related strain. Since this nucleic acid is characteristic of cell nuclei, further analyses are indicated.

Thus it is seen that the structure, the attributes of reproduction, and mutation of viruses can be and are being submitted to analysis by scientific experiment, and one can be intrigued by the speculation that results of the most fundamental nature for biology are in the making. With the labile nucleoprotein molecule or molecules of the smaller viruses now accessible to study, one might perhaps not improperly indulge the thought that in this realm of small things an evolutionary growth in structural and functional complexity of chemical molecules of protoplasmic origin might possibly lead to the acquisition of the attributes of multiplication and mutation if not eventually toward a self-sustaining state by a gradual development of elements of an essential metabolism, after the fashion of true microorganisms. One might even indulge the fancy that a degrading microorganism might reach a state of similar unbalanced equilibrium where reversal of retrogression might be possible.

These illustrations of twentieth century research in the field of infectious disease are sufficient to indicate what to me appears to be fundamental issues. The problems seem sharply enough defined and a great new array of knowledge and method is available for pursuit of their solution. No promise of utility should be required for continuous support of competent inquisitive interest in such problems. They will never be quite solved because they have to do with the very elements of life.

Reactive Groups of Proteins in Diagnosis

Charles Huggins, M.D., D.Sc.
Professor of Surgery
The University of Chicago, Chicago, Illinois

I travel along a well trodden path which was discovered by the Bixby Professor of Surgery at Washington University. Evarts Graham was the first to appreciate how much chemistry could contribute to the advancement and understanding of surgery.

The peculiarities of the structure of proteins are such that they may be utilized to good advantage for diagnostic purposes. This paper is concerned with surface activities of proteins; to keep the discussion within manageable proportions the enzymatic activities of those surfaces are not included. The methods are based on reactions which are not harsh enough to destroy the protein molecule. The investigation of reactive groups of protein surface by these methods is new and has, I believe, great potential as a diagnostic agency. Diagnosis in this system is at the molecular level.

The aim of science, as I understand

it, is to provide an analysis based on as accurate data as may be obtained, and if the analysis is a penetrating one, it is great science.

In no area of medicine has the lack of precise measurements been as glaring as in cancer research. The growth of a cancer is frequently so insidious and diffuse, while progressive, and the available investigative methods in the past have been so inadequate that often the only significant numeral to emerge from a careful clinical study was unity—an addition to an already long mortality table.

A great deal of work is now being done to develop chemical methods for recognizing the activity of neoplasms in living organisms, and it appears that some progress is being made. The importance of studies of activities in medicine are obvious especially in obtaining clues for experimental therapy and in evaluating results; there is a very ancient philosophic concept perhaps germane to investigations of activities in disease which Balzac has stated neatly, "Dieu est le mouvement, peut-etre." An inactive tumor kills nobody.

Those giant molecules of nature, the proteins, with their great diversity of structure and activity, are assuming with each year an increasing importance in the deeper understanding of medicine. The proteins are characterized by a tremendous chemical versatility, and further they are the most specific compounds in nature. The carbohydrates, fats and salts are much alike in all people. The personality of man depends largely on his proteins: in all forms of life these bodies furnish the chief differentiating characteristics of the tissues and the sum total determines the individuality of the organism as well. The proteins are concerned in every functional activity of the cell.

Now the specific characters and functions of proteins in their seemingly infinite variety depend not upon highly complex organic structural forms but on different numbers and sequences of rather simple and weak dipolar compounds, the α-aminocarboxylic acids as was shown by that great chemist Emil Fischer (1906); of these twenty-five amino acids are known. As an analogy comparing these twenty-five constituents of proteins to the letters of the alphabet, one readily notices that variations of the order and number of the letters alone decide whether the product is a sonnet or the telephone directory. Nature's incorporation of amino acids in proteins, however, is something like a super-Slavonic language where the words are very long.

The acidic group of one amino acid unites with the basic group of another with the loss of a molecule of water to produce a chain of residues in which the different side groups are arranged like "differently coloured beads strung on a necklace, the polypeptide chain." To extend the simile, some of the side chains are precious stones and others are glass, the jewels being the more reactive groups.

The concept of folding or a spiral structure of the polypeptide chain in native proteins is fundamental in understanding their properties; this deduction of *physical* shape of the molecule was first made by Astbury and

Street from a study of hair, the protein of which is arranged in a long filament. Upon heating a hair it was demonstrated that the fiber could be stretched about 30 per cent, and these workers attributed the phenomenon as being due to the elongation of an intra-molecular group. Since the process was reversible clearly the peptide chain was not broken. In this classic paper it was deduced that the long fibrous protein molecule of hair involved the countinuous repetition of hexagonal ring systems connected by bridge atoms which were disrupted by heating. The bridges now are generally considered to be hydrogen bonds, being a rather weak association in this case between N, H, and O having about one-eighth the strength of a covalent bond.

While in most of the residues the side chain is neutral as in alanine,–CH_3, some of the amino acid residues such as glutamic and aspartic acids are negatively charged while others bear a positive charge as occurs with arginine, histidine and lysine. Utilization of reactive groups in diagnosis is at present confined to those side chains of albumin and globulin bearing the sulfhydryl radical $-^{S}H$, or electrically charged groups.

Much is known about serum albumin. It has a molecular weight of about 69,000. It contains about 586 residues (beads on the necklace), of which 109 are cationic with a positive electric charge and 93 are free carboxyls with a negative charge. One of the groups is sulfhydryl, as was deduced by W. L. Hughes, Jr., by working with metallic compounds (dimers) of albumin, and this single jewel has special properties among its 585 associates.

The work of my associates, Dr. E. V. Jensen and Mrs. A. S. Cleveland, on reactive groups of proteins began with a study of two long known, but still unexplained, effects: in most patients with cancer the amount of albumin in serum is low and the serum also has less reducing power than normal serum. Purr and Russel studied the proteolytic enzymes papain and cathepsin which they had inactivated by dialysis against water, this treatment having been found effective in removing sulfhydryl groups essential for the activity of these enzymes. The activity of enzymes inactivated in this way could be restored by adding blood. The addition of normal blood was more effective than cancer blood in regenerating enzymatic activity. The effect has since been found to concern the plasma. Moreover cancer often reduces methylene blue at 100°C. more slowly than normal serum.

Our experiments may be summarized briefly. We investigated the formation of a gel in serum at 100°C. Undiluted serum from every person, well or ill, coagulates under these conditions and every human serum on the other hand can be diluted to a point where it will not solidify on boiling; for example, a drop of serum dissolved in the waters of the Mississippi could not reasonably be expected to form a gel on boiling the mixture. It was found useful in diagnosis to measure the extent to which a serum can be diluted without losing its ability to form a gel on heating, determining thereby the least coagulable percentage of serum. The technique has

great precision and reproducibility. In brief, serum is mixed with M/15 phosphate buffer, pH 7.4, in a Wassermann tube and immersed in boiling water for thirty minutes. The technique was standardized in a very simple way. A rigid definition of a gel was set up based on its ability to remain on a wire screen of standard (No. 8) mesh; it is a "go or no go" method. Whenever a gel does not form in concentrations of serum, twenty-one per cent or less, that serum comes from a person with a significant abnormality of the serum proteins.

Moreover the value of the data was extended by relating the lowest percentage of coagulability to the protein content of the serum; the lowest coagulable protein concentration (LCPC) then is the least coagulable percentage multiplied by total protein content of serum in grams per cent. The deficiency in coagulation may concern the total quantity of normal protein and also the quality of the protein. In cancer the serum albumin is frequently abnormal in kind.

In our studies the least coagulable concentration of serum protein (LCPC) of normal persons was always less than 1.39 grams per cent. In the abnormal range of 1.39 or larger several clinically significant categories of disease were found: (a) 85 per cent of a consecutive series of patients with cancer; (b) most patients soon after a surgical operation of magnitude; (c) all pregnant women when the duration of pregnancy had been 12 or more weeks; (d) about one-third of patients with a miscellaneous group of grave illnesses. In the last group repeating the results within a few days sometimes showed a lowering of the value.

It is of interest that nearly all patients with cancer have detectable abnormalities in serum proteins and that often a small cancer produces as extensive defects as the great growth processes which follow conception. Thermal coagulation of serum is not a test for cancer; it so happens that most patients with cancer have a defective capacity of the serum to gel on heating.

Now this non-specific effect has significance in three directions; a limited value in diagnosis, considerable importance in determining prognosis, and also it is a little step forward in pure science.

The effect is certainly quaint and a little bizarre. Does it have any meaning? It was necessary to look into the nature of gels which occur when proteins are heated. A heat-induced coagulum is an everyday phenomenon in the practice of the culinary arts. We see it each morning in the breakfast egg.

A gel consists of a cross-linked three-dimensional network of long molecules capable of binding a large amount of solvent within its frame work. For any given volume of solution there is a minimum number of protein molecules required to build a network which can hold all of the water present. If the protein is less than this critical amount, the solution after heating will remain liquid; this is the basis for recognition of low albumin values. The gel formation in blood serum depends chiefly on the albumin content influenced somewhat by the gamma-globulin present;

alpha- and beta-globulins do not heat-coagulate.

Depending on the pH of the solution heat-denatured serum albumin forms two essentially different types of gels which may be designated as clear or cloudy clots. Cloudy clots form in the region of pH 4.8 – 6.0 in a matter of seconds with a low protein concentration; these clots bind water poorly. Clear clots form below pH 4.5 and above pH 6.0, after some minutes of heating and in a relatively higher concentration; they possess a marked capacity for hydration.

By X-ray diffraction studies Astbury, Dickson and Bailey have shown that heated egg white films consist of parallel bundles of elongated polypeptide chains; no doubt coagulated serum albumin is similar.

Mirsky and Pauling postulate that thermal denaturation of a protein involves the breaking of hydogren bonds which hold the native protein in its specific configuration causing an unfolding and extension of the molecule; the coagulum forms by linkages through new hydrogen bonds between carboxyl and amino groups of neighboring polypeptide chains. To account for the differences in two types of albumin clots we assume that there are two types of aggregation: network formation by attachment of the molecules at a few essential points, and an additional more extensive lateral association of the chains. In the region of the isoelectric point, intermolecular repulsive forces are minimal so that aggregation of extended chains can take place rapidly and at many points forming dense thick fibers that are unable to hold much water. As the pH is raised or lowered from the isoelectric point there is a progressive increase in the net charge (negative or positive respectively) with a consequent increase in the intermolecular repulsion resulting in thin fibers fixed at a few points and containing much water between them. Consequently they are translucent, well hydrated clots. The deficient ability of serum albumin in certain diseases to gel on heating is ascribed to the presence of a foreign molecule bound to its charged groups interposing a barrier to hydrogen bond formation or other new association.

The effect of electric charge on protein coagulation appeared in some other experiments as well as attempting to correlate the deficient reducing powers of cancer serum with defective coagulation. Small amounts of propyl mercaptan and other sulfhydryl compounds greatly enhance the rate of thermal coagulation and induce clots in previously incoagulable albumin solutions. Conversely we observed that halogenated acetates, of which iodoacetate is the most effective, having the peculiar property of preventing serum albumin from forming a gel when heated. Iodoacetate and iodoacetemide are alkylating reagents for proteins, reacting with sulfhydryl and amino groups. This compound iodoacetate, promotes rather than prevents denaturation of protein. It blocks the association of extended chains because of the introduction into the molecule of new carboxyl groups which increase the net negative charge and hence furnish new centers of intermolecular repulsion.

The serum of most patients with cancer, and that of a considerable number with other diseases as well, requires less iodoacetate to prevent coagulation by heat than is required for a similar effect on normal serum containing the same quantities of total protein or albumin present: the data may be related in the form of an iodoacetate index which supplements usefully the determination of the amounts of proteins present. Smaller amounts of iodoacetate prevent association of abnormal albumin than are required for the normal kind because there are already negative charges on the proteins.

Further information about available groups of serum albumin was obtained by studies of its capacity for the binding of anions. This property of albumin was discovered by Arthur Grollman in 1925 using the dye phenol red. Since then many cases have been described where albumin forms complexes with organic and inorganic anions, many with considerable physiologic and pharmacologic activity. The studies have led to the physiologic concept of the transport function of albumin. B. D. Davis and W. B. Wood (1942) discovered that sulfonamides were carried in the blood, in part bound to albumin. Albumin is characterized by an unusual property among proteins. It combines with dye or other anions on the basic side of the isoelectric point, although each carries an overall negative charge. There is good evidence, largely obtained by I. M. Klotz, that the small anions are bound to proteins in two ways, namely through electrostatic fixation and by molecular attraction of the van der Waals type. Electrostatic attraction apparently occurs through the anions with their negative charge and the cationic residues of the basic amino acids in the side chain residues, particularly the ε-ammonium group of lysine and less significantly with arginine.

Now the decreased thermal coagulation of cancer serum is interpreted as indicating a smaller number of electrically charged groups in the albumin molecule. The deficiency of anionic dye binding is further evidence for this theory which it extends since it implies a decrease of positively charged centers. It was possible to take another step forward. The defective coagulation and poor binding of anions was eliminated by fractionation of the proteins in cold ethanol by the method of Cohn et al.; following this treatment no differences could be found between the serum albumin of normal and cancerous persons. The cancerous albumin is restored to normal.

These facts are best explained by the solvent action of alcohol on an abnormal group, presumably of anionic character bound to the albumin molecule in cancer. The nature of these groups has not been identified.

In summary, investigation of reactive groups of proteins by methods not drastic enough to disrupt the molecule reveals important defects in serum albumin in many patients with cancer. Evidence of an abnormal albumin is present. The facts are best explained by postulating that abnormal molecular structures are fixed to cationic centers of albumin in malignant disease and in certain other states as well.

Some Observations on Bone Growth

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I give briefly some observations on bone growth, made by Dr. Richard Follis and me in the course of our studies of children dying in the Harriet Lane Home from all manner of causes. Since the conditions and diseases which resulted in the death of these children are known, the cases furnish natural experiments.

The bone grows in length as the result of the proliferation of the epiphyseal cartilage. Growth in thickness is caused by the bone-forming cells, known as osteoblasts. Achondroplastic dwarfs are living demonstrations of the separation of the activities of cartilage and bone cells. The bones are short, because cartilage with the power to grow is not there, but they are sturdy because osteoblastic growth is unimpeded. In achondroplasia the dissociation between bone and cartilaginous growth depends on an inherited defect of the cartilage and is permanent, but temporary dissociations occur in normally-formed children in the course of illnesses, and it is about these temporary dissociations that we wish to speak.

We know little concerning the mechanisms which govern the growth of bones, but we do possess various isolated facts bearing on the subject:— The growth of the cartilage falls to a minimum after the removal of the hypophysis and also after the removal of the thyroid, though not abolished altogether, and it can be revived again through the administration of the respective hormones of these glands. The parathyroid glands affect osteoblastic activity. The androgens also influence cartilaginous and osteoblastic growth. But endocrine regulation of bone growth is too confused a topic at present even for speculation. We scarcely know more than that certain glands are actors in the drama. The exact roles and interrelations are little better than surmises, and the plot in completely obscure.

It is certain that both cartilaginous and osteoblastic activity are profoundly influenced by nutritional conditions, as would have to be the case since cartilage and bone cells are living and, quite regardless of functional requirement, are dependent on nutriment. Infantile paralysis furnishes an illustration of the dependence of both these kinds of cells on an adequate nutritional supply, for, whereas the bone of the paralyzed limb becomes extremely thin and lags behind the healthy limb in length, growth can be stimulated and started again, though to a limited degree, if the blood supply is improved.

It should be pointed out further that growth in length is fundamentally different from growth in thickness; the latter is obligatory in the sense that it is required to meet the demands of stress and strain and we know that new bone formation and the destruction of

old bone, that is the activity of the osteoblastic group of cells, is under the control, to an extraordinary degree, of the mechanical factors of stress and strain. Growth in length, on the other hand, is not required to meet stresses and strains, but has a genetic basis. The reason, however, that we are so positive that the regulatory mechanisms which govern cartilage and bone growth can operate separately is that the evidence at times is written in the bone structure itself. But before presenting this, it is necessary to give a brief explanation concerning obsteoblastic function.

It is wrong to think of osteoblasts as being exclusively bone-building cells and of osteoclasts as being of a totally different kind and that bone is destroyed solely by osteoclasts. Osteoblasts are cells possessing a reversible action. There is no question that osteoblasts form bone. However, single osteoblasts can and do destroy the bone surfaces against which they lie and one finds almost always disorderly groups of osteoblasts where bone destruction is considerable. Osteoclasts may be the only cell present in an area of destruction but they may not be present at all. Osteoclasts appear to be osteoblasts aggregated in giant cell form and they undoubtedly exact a powerful lytic action on bone matrix. At any rate, the trabeculae of bone in the shaft are built upon or new ones formed by the osteoblasts and, conversely, trabeculae are partially or completely destroyed by these same osteoblastic cells. At the cartilage-shaft junction, it is through the agency of the osteoblasts with the accompanying capillaries — we cannot separate the activities of the osteoblasts and capillaries—that the capsules of the cartilage cells and the intervening matrix bridges are dissolved and penetrated, and it is also through the agency of these calls and the blood vessels that certain parts of the bared framework of calcified matrix are covered over with bone and other parts are destroyed. These constructive and destructive processes at both the cartilage-shaft border and in the shaft proper may occur at microscopical distances from each other on the same trabecula and, when it is considered that the same kind of cell is responsible for both, any hypothesis concerning the directing forces is baffling.

When one examines the end of a rib or a limb bone in a rapidly-growing child who has died of a severe illness of ten days or more duration, it is common to find at the end of the bone a quite distinctive formation. (Fig. 1.) The formation is composed essentially of a dense framework of calcified matrix substance of the cartilage in the interstices of which are found large numbers of intact cartilage cells. The formation may be as long as the entire proliferative zone of the cartilage. We shall refer to this structure, as it is seen in histological sections, as a lattice. Its characteristics are these: It has the pattern of the cartilage, for it is nothing less than the cartilage which the capillaries and osteoblasts have failed to invade and render into shaft. It so happens that hematoxylin stains calcified matrix substance a deep blue, but fails to stain bone matrix for reasons which have never been satisfactorily ex-

Fig. 1

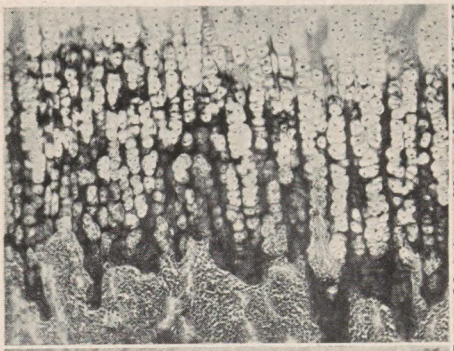
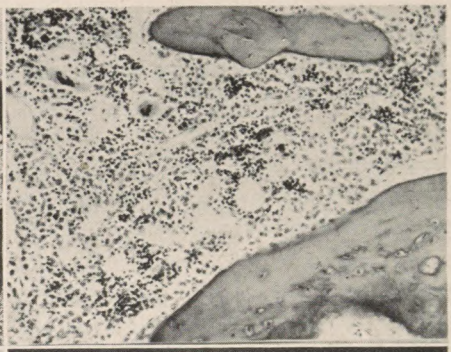


Fig. 2



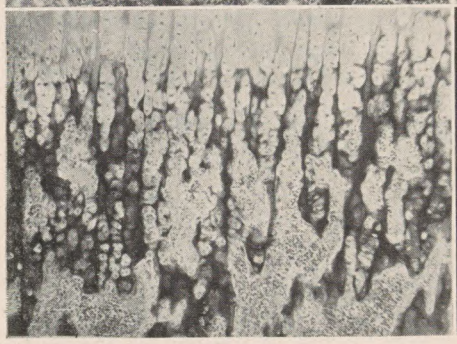


Fig. 3

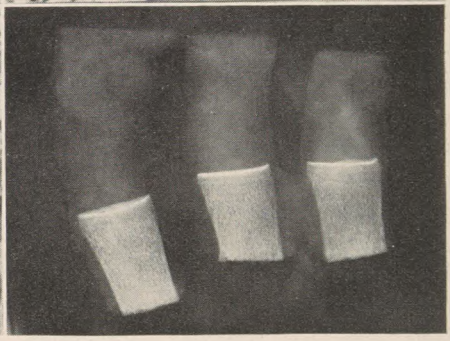


Fig. 4

Fig. 1. A typical lattice of calcified matrix substance with imprisoned cartilage cells. This non-specific type of lattice formation due to the continued growth of the cartilage, on the one hand, and on the other the continued failure of osteoblasts and capillaries to invade and remodel it into bone, casts a shadow in the X-ray film similar to the shadows seen in scurvy, congenital syphilis and lead poisoning. (See Fig. 4.)

Fig. 2. Trabeculae in the shaft in a case of lattice formation at the end. Arrest of growth of the trabeculae is evidenced by the absence of osteoblast rows on the edges and absence of their product, "physiological osteoid." The lining osteoblasts have in reality been reduced to a thin membrane where it has been accidentally pulled loose in the process of sectioning (the lower trabecula, upper border on the right side of the photograph).

Fig. 3. Lattice which is in process of being channeled by the blood vessels and osteoblasts. The invasion of the lattice when it occurs is always irregular due to the fact that vessels succeed in breaking into it at some points and remain blocked at others. When this irregular invasion of the lattice is extensive, the lattice may be broken up into fragments. As the result of bone formation on the fragments giant trabeculae are formed. (See Fig. 9.)

Fig. 4. Ribs showing dense shadows at their ends cast by the lattices which have resulted from growth dissociation between cartilage and bone. The shadows cast by these non-specific lattice formations are usually thinner than those seen in well marked lead poisoning.

plained. Eosin stains bone matrix a contrasting pink. These stains show that the lattice consists essentially of calcified matrix framework of the cartilage together with many retained cells, but the framework itself is much coarser than that seen under normal conditions and the calcifiction of the framework is also heavier and often extends into the horizontal cross bridges of matrix substance which separate the cartilage cells. Examination shows, too, that the osteoclasts in the lattice interstices are few in number, and it also reveals evidence of their inactivity because there is little new bone formation. It also shows that the blood vessels are few and have succeeded in penetrating the lattice in only its lower part, and there only irregularly. When one turns to the shaft, one finds strong corroborative evidence of the failure of cellular activity. (Fig. 2.) The obsteoblasts lining the shaft are few and have become flattened so as often to be seen with difficulty, and there is little or no evidence on the surfaces of the trabeculae that fresh bone formation has occurred in the form of "physiological" osteoid. The obsteoblastic covering of the trabeculae is often reduced to a barely visible membrane. With the suppression of obsteoblastic activity, osteoclastic activity is also suppressed. The whole process of cellular activity in the bone in both directions has been reduced to a minimum.

It is apparent that the lattice formation which we are describing can be interpreted only as the product of the combination of the continued growth of the cartilage and failure of the shaft forces, namely the osteoblasts and the blood vessels, to invade, remodel and convert the accumulated cartilage into shaft. In rickets the cartilage keeps growing and, as the result of the general disorganization of the growth processes at the cartilage-shaft junction, conversion into bone is impossible and the cartilage becomes massed at the end of the shaft. The situation in regard to the lattice formations in the bones of non-rachitic children is analogous, but in them it is the nonrachitic calcified cartilage which accumulates.

Some comments are now required. The cartilage has a dense, almost solid, structure. The density of the lattice is due to the fact that the cartilage frame has been retained with a large part of its cells, i.e., it has not been invaded, cleared of its cells, opened up by destruction of its structurally useless parts and the remainder remodeled into bone by the osteoblasts and capillaries. But the appearance of density is increased because the matrix framework is actually thicker than normal, and because the calcification of the framework is denser and more widely extended than normal. When cartilage remains in contact with the shaft elements for some time, the calcification always becomes more dense and more widely distributed than when growth is rapid and the matrix substance remains in contact with the osteoblasts and capillaries for briefer periods. The extensiveness of the calcification of the lattice, and probably also the excessive production of the matrix substance itself, indicates that the growth of the cartilage has been slowed, i.e., it has not been normal, although it has not stopped.

From the stereotyped description given it must not be thought that lattice formation is uniform. The rate of growth of the cartilage at the different bone ends is subject to great variation. It is most rapid in the middle tier of ribs and it occurs most slowly, from among the long bones of the extremities, at the upper end of the ulna. Moreover, the rate of growth of the cartilage must vary from child to child and it is much less rapid in older children than in infants. It is obvious that if the growth of the cartilage is slow the lattice which is produced will be short. In the fast growing rib, the lattice may be extremely developed, whereas at the upper end of the ulna it is so short as not to be recognizable as a lattice. If, too, the growth of the cartilage at a normally fast-growing bone end is slowed from illness or any other cause, the lattice produced will be short. Turning now to the other variable, if osteoblastic and vascular activities are only partly suppressed, the lattice may be quite extensively invaded and, in the invaded parts, turn into shaft. (Fig. 3.) In the most marked instances of lattice formation, such as we have pictured, the architecture of the lattice is the pattern of the cartilage almost completely undisturbed. But in proportion as the destructive activity of the shaft is preserved, the lattice is invaded and disrupted in the part bordering the shaft; it may become deeply channeled and in some instances it has been so heavily attacked that it exists only in fragments. The situation is further complicated because the time factor enters. If the factors essential for lattice production have existed for a short time, lattice production will be small.

Lattice formation occurs in congenital syphilis and in scurvy and is an essential feature of the lesion of the bones in these two diseases. The cause is fundamentally the same as in this nonspecific kind of lattice formation just described. The lattice in scurvy is due to the continued growth of the cartilage in the face of an almost complete loss of osteoblastic function, and is the best example of dissociation of this kind in the two processes. Follis has recently given proof that the osteoblasts in scurvy are abnormal by showing that they are lacking in phosphatase but that, as soon as vitamin C is administered, they rapidly acquire a phosphatase content and begin to resume their fibre-forming function.

The question arises if the lattice which develops in severe illness might not be due to a vitamin C deficiency brought about by exhaustion of the vitamin. Follis' and my studies have shown that rickets is a frequent terminal development. We think it improbable, however, that the lattice formations which we have described depend on a vitamin C deficiency because they can develop in breast-fed infants and under supposedly adequate vitamin C administration. But we cannot be certain that a vitamin C deficiency can be excluded as a possibility. The reason for the osteoblastic inactivity in congenital syphilis has never been satisfactorily explained.

Lattices develop also in lead, bismuth and elementary phosphorus poisoning, but these are all bony and are of an

entirely different nature anatomically from what we have described.

To pediatricians, the fact that a lattice may develop as a by-product of any severe illness will be of interest, for lattices cast shadows in x-ray films and often their presence has raised the question whether scurvy, syphilis or lead poisoning must not be invoked to explained them. (Fig. 4.) Often we believe the lattice of severe illness has been mistaken for the lattices of these other conditions.

Soon after radiography made possible the study of the finer structure of bones, the so-called transverse lines were observed in the x-ray film and it was noted that their occurrence could be dated with acute illness. Indeed the dating proved to be so exact that transverse lines have been used to prove that the growth of bone in length is not due to interstitial growth in the shaft, and also to measure the rates of growth of the various long bones. What are these transverse lines anatomically? Actually they are not transverse lines at all, but transverse strata which appear as lines in the x-ray films because they are caught on edge when the bone is laid parallel to the film surface. The strata are composed of horizontally directed trabeculae, some of which join and form an interlacing network. They in their turn are produced by dissociations between the growth of the cartilage cell and the osteoblast, this time the cartilage cell being the negative and the osteoblast the positive factor.

The general principle determining the development of these strata of horizontally-disposed trabeculae is that, when the growth of the cartilage stops, the osteoblasts are unable to expend their growth energy in the vertical direction and are forced to expend it laterally along the under surface of the cartilaginous plate. The steps appear to be as follows: When the cartilaginous growth stops, the capillaries with their attendant osteoblasts penetrate all the cartilage cell capsules of the provisional zone which are ready for penetration and in so doing bare the walls of matrix substance. They then reach the living cartilage cells, but these are resistant and cannot be broken into. The capillaries and osteoblasts there find further progress in the longitudinal direction blocked and are compelled to spread out laterally in all directions under the under surface of the cartilaginous plate. As a result of the blockage of their forward progress the osteoblasts become concentrated on the exposed walls of the matrix framework and layer them over with bone. The bone formation occurs in the horizontal plane because, owing to the barrier furnished by the under surface of the cartilaginous plate, the horizontal plane is the only one affording space for growth spread. Additional factors may enter in. We have often observed in rickets, scurvy and congenital syphilis that proliferative cartilage which has been exposed to the shaft environment for some time tends to develop a thick matrix border. The stagnation of the capillaries and osteoblasts along the under surface of the cartilaginous plate may well increase the formation of matrix substance for the osteoblasts to build upon. With the stagnation, calcification of the matrix

Fig. 5 Fig. 6

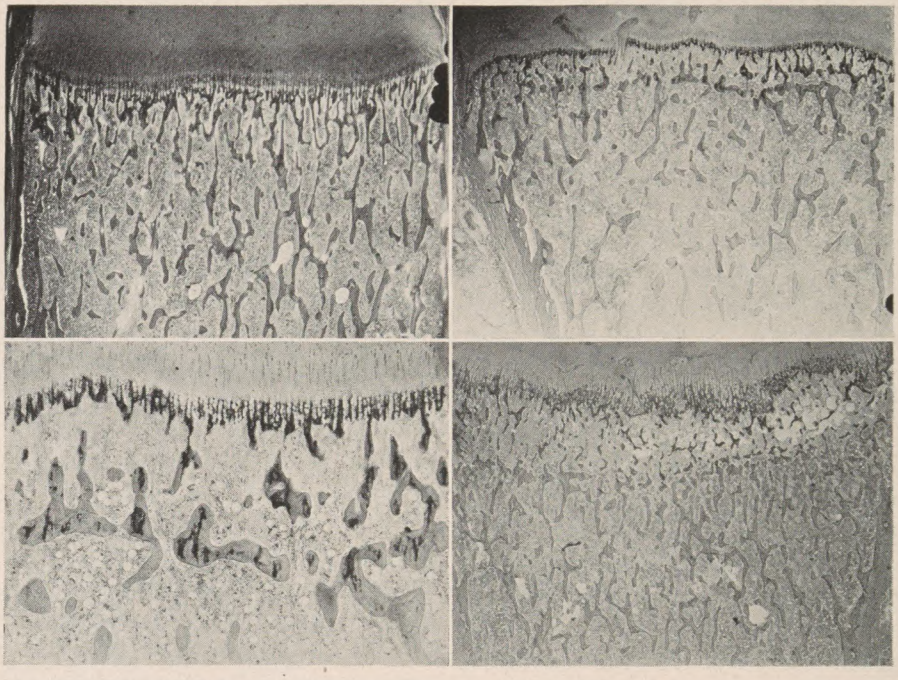


Fig. 7 Fig. 8

Fig. 5. A transverse stratum composed of horizontally directed trabeculae lying just under the cartilage. The cartilage has receded from it just enough so that its upper demarcation is visible.

Fig. 6. Transverse stratum extending all across rib. This, as is always the case, formed at the cartilage junction. It occupies the exact position in which it was formed but owing to growth of the cartilage new shaft has formed beyond it, so that it lies well away from the cartilage in the shaft substance.

Fig. 7. Transverse stratum seen in Fig. 6 but higher magnification. The nature of its composition is evident. The black interior parts are the calcified matrix partitions of the cartilage on which the osteoblasts settled when new formation (growth) of cartilage stopped. The grey is the bone which the osteoblasts formed, using the calcified matrix as a base. The stratum has a horizontal direction because owing to stoppage of cartilaginous growth the horizontal plane was the only one offering space for new bone formation.

Fig. 8. The transversely directed and misshapen trabeculae at different levels show that a succession of disturbances in longitudinal (cartilaginous) growth occurred in the child from whom this bone was taken. There is evidence of one severe arrest consisting in the stratum extending all across and of many minor arrests shown in isolated horizontally directed trabecular formations and in the many instances of deformed trabeculae.

substance undoubtedly extends and becomes more dense, but calcification is not a factor in tranverse stratum formation because this anomaly occurs with great frequency in rickets in which disease calcification is defective. Osteoblasts seek out, preferentially for purposes of bone formation, small nooks in the framework of calcified matrix substance, such as the empty capsules of the cartilage cells where they find themselves effectively walled in. This apparent peculiarity of the osteoblasts may also be a factor in transverse stratum formation. At any rate as the horizontal trabecular formations approach each other, we have repeatedly observed that the osteoblasts get in between and complete the junction. In all probability, growth of the cartilage is rarely completely halted, i. e., a slight degree of growth with consequent slow maturation of the under surface of the cartilaginous plate continues to occur, and this slight degree of growth may favor the development of thicker transverse trabecular formations by furnishing an increased amount of horizontally-disposed matrix framework for the osteoblasts to settle upon.

Transverse strata which extend all across the bone always start at the cartilage-shaft junctions. (Fig. 5.) Moreover they always occupy the original positions in which they were formed. When one encounters a transverse stratum well down in the shaft of a long bone, the explanation is merely that the cartilage has grown away and left it in its wake. (Figs. 6 and 7.) In the slow-growing bones, the transverse strata will be found close to the cartilage, whereas in the rapidly-growing bones they may be separated by some distance. Although transverse strata formations always start at the cartilage-shaft junction, they frequently continue to progress after the growth of the cartilage has been resumed. Often we have observed that a transverse stratum well down in the shaft is continuing to develop as the result of continued osteoblastic activity. Sometimes the osteoblasts are bringing the horizontal branches of the trabeculae together by a process of appositional bone formation, sometimes by membraneous bone formation, sometimes by both processes in combination.

Often under the microscope, it is possible to see evidence from the many telltale transverse strata in the substance of the shaft, that checks of cartilaginous growth have been occurring one after the other for a long time. (Fig. 8.) These strata may stretch entirely across the shaft, in which case they appear as transverse lines in the x-ray film, or they may be limited to small groups of trabeculae here and there. It is common to find in the substance of the shaft another evidence of growth disturbance in the form of giant trabeculae which, however, have a different origin than the transverse strata just discussed. (Fig. 9). Giant trabeculae are formed merely from chunks of lattice which have been cut off intact to be later filled in and covered over with bone as the result of continued osteoblastic activity.

Transverse strata of horizontally-disposed trabeculae are exceedingly common in the growing bones of children. It is common to find them in the

Fig. 9 Fig. 10

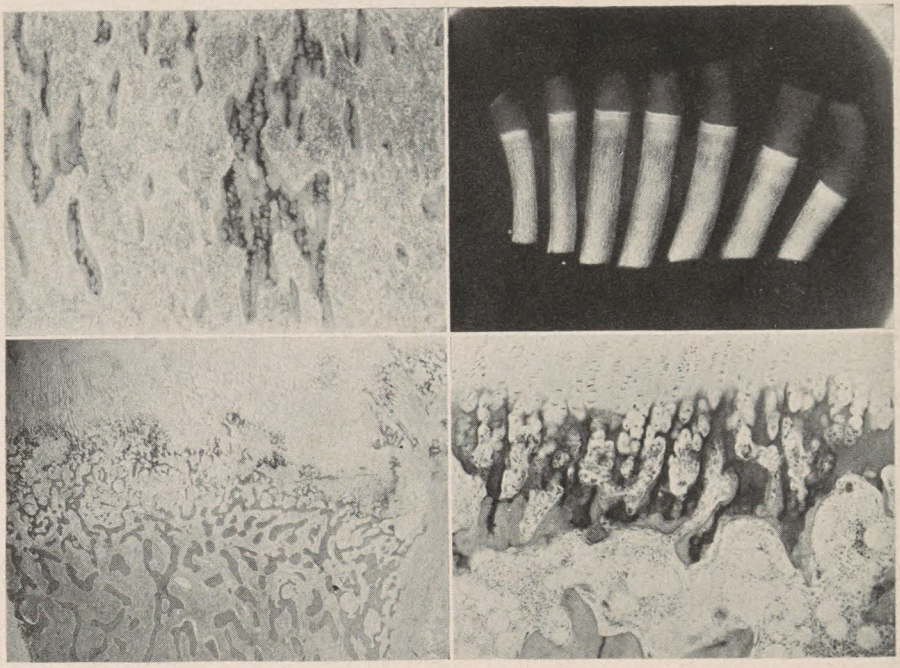


Fig. 11 Fig. 12

Fig. 9. An example of a giant trabecula formed as the result of bone formation by the osteoblasts on a chunk of lattice. The chunk was produced by irregular invasion of a lattice. It represents a piece of lattice which escaped invasion or was cut off and which the osteoblasts after destroying the contained cartilage cells then filled with bone.

Fig. 10. "Transverse lines" in the X-ray film of a tier of ribs. As explained in the text these lines or shadows are cast by the strata of horizontally branching trabeculae in the shaft substance. The film shown is from the infant of Figs. 6 and 7.

Fig. 11. A transverse stratum marking the beginning of an acute severe rickets in which calcium-phosphate deposition in the cartilage stopped suddenly all across. When rickets is mild, transverse strata are not produced. The cause of transverse stratum formation in rickets is really different from that described. The rachitic cartilage next to the shaft having lost the support of the calcified matrix collapses and furnishes a barrier to the advance of capillaries and osteoblasts. Unable to advance these spread out laterally and produce rachitic bone (osteoid) on the under surface of the mass of cartilage, encasing the latter. The principle of formation is the same but the barrier furnished by the cartilage is not due to growth cessation, though this may be present too, but the impenetrability of the cartilage resulting from the rickets.

Fig. 12. A transverse stratum on the under surface of a lattice. The stratum started at the cartilage junction. Then osteoblastic growth became halted and the cartilage resumed growth. The result was both formations, a lattice with a bony transverse stratum on its under surface. First one dissociation occurred, producing the stratum, then the reverse producing the lattice.

X-ray film. (Fig. 10.) Birth is regularly marked in the long bones by the appearance of a stratum showing where intrauterine growth formation stopped and postuterine began. The acute onset of severe rickets is commonly marked in the bone by the formation of transverse strata (Fig. 11), and it is common to find a transverse stratum on the under surface of a lattice, meaning that the first shock of the infection produced a temporary check in cartilaginous growth which the osteoblasts promptly inscribed. (Fig. 12.) Lattice formation requires time and is the result of a growth disturbance of a number of days or weeks. Dysentery and the severe pneumonias following whooping cough, formerly diseases of extreme severity in infants and lasting in fatal cases for three to six weeks, have almost regularly produced extreme degrees of lattice formation in the cases of our study. The occurrence of transverse strata in bones, on the other hand, may be the result of illnesses of a very temporary and not very severe nature and indicate that the mechanisms which preside over the growth of cartilage must be adjusted with a great delicacy. They are evidence that the cartilaginous growth must be subject to sudden halts and equally sudden resumptions and also that the genetic urge upon the cartilage for growth fulfilment must be powerful, since it is so persistent under conditions under which the osteoblasts at least become incapacitated. Lattice formations differ also from the transverse strata in that, when osteoblastic activity is resumed, they are remodelled and removed. Neither lattice nor transverse stratum formations can be regarded as scars. The transverse strata are examples of abortive or misdirected growth, and the lattices as partial growth processes to be completed as soon as osteoblastic activity is resumed.

Doubtless all growing tissues in the body are subject to similar growth disturbances but only in the bone are the time sequences preserved.

Robert S. Brookings

by Philip A. Shaffer, Ph.D.

Distinguished Service Professor of Biological Chemistry
Washington University School of Medicine

To honor the memory of Robert S. Brookings on the Centennial of his birth by recalling his unique contribution to the creation of this Medical School on its 50th Anniversary is a double privilege, one which I might appropriately share with Robert Terry and Joseph Erlanger, who likewise have been members of the faculty from its establishment. We and a few others can testify from first-hand knowledge about the conception, the infancy and the youth of this institution—now of adult stature.

Dr. Terry will speak, I understand, of the early history and academic ancestry of our Medical School, including its *first* reorganization in 1899, the date

Scenes of the 50th Annive

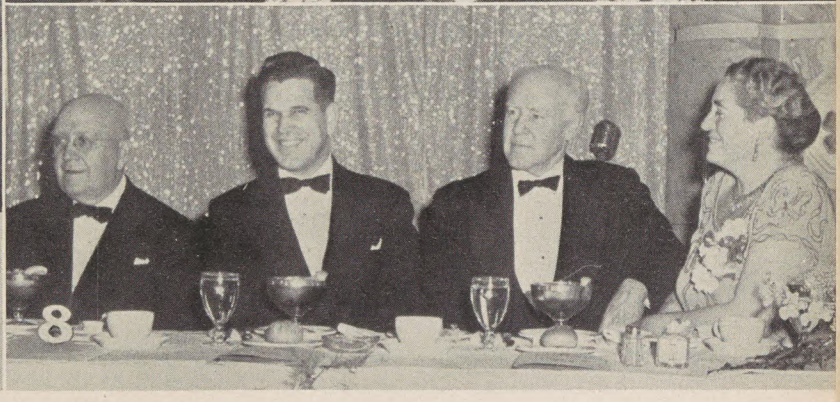
1. Following his address, Dr. Gregg receives congratulations from Mr. Edgar E. Rand, chair man of the Barnes Hospital Board of Trustees. Others in the group are Dr. Robert A. Moor M.s. Robert A. Holland, and Mrs. Arthur H. Compton.

2. Receiving honorary degrees at the Convocation marking the centennial of Robert S. Brook ings' birth were: Dr. Ernest W. Goodpasture, Dr. Abraham Flexner, Dr. Edwards A. Park and Dr. Charles Huggins.

3. Scene in Graham Chapel during the special convocation honoring Robert S. Brookings an the Medical School Anniversary.

4. Dr. Alan Gregg, main speaker at the dinner, leaves the speaker's table after the program taking the souvenir booklet with him.

5. Dr. Harry Brookings Wallace, president of the Washington University Corporation, applie



the School of Medicine

ar to the cornerstone of the new cancer research building, while Chancellor Arthur H. pton watches from the left.

Among alumni attending the 50th Anniversary Dinner were: from left to right, Dr. Archie arr '21, Mrs. Carr, Mrs. Melvin A. Roblee, and Dr. Roblee '25. On the other side are left to t, Dr. and Mrs. James H. Scruggs, Jr., and Mr. and Mrs. William A. Groiock.

Conversing with Dr. Abraham Flexner, center are Dr. Philip A. Shaffer, former dean, and Robert J. Terry '95, professor emeritus of anatomy.

Those at the speaker's table included Dr. Harold G. Moulton, president of the Brookings titution in Washington, D. C.; Dr. J. R. Heller, Jr., chief of the National Cancer Institute, esda, Md.; Dr. Alan Gregg, director of the Division of Medical Sciences, Rockefeller Founda- and Mrs. Arthur H. Compton.

now selected for its birth certificate. We have sometimes claimed the year 1840 for its genesis, but it was the reorganization in 1899 in which Mr. Brookings first made his entry in medical education. It is said that his diplomacy and persuasion were decisive factors in uniting the rival schools, thus accomplishing the first reorganization.

My remarks will concern the rare vision and inspiring leadership of Mr. Brookings in first conceiving and then creating the present medical school and the medical center of which the school is the hub. Many here this evening may not realize how novel and farsighted that undertaking was at that time. To many the story is familiar and was related in part by Dr. Moulton at the Convocation this morning. I shall tell it once again, briefly and based mainly on my personal knowledge. First, may I note that the presence in this gathering of Mrs. Robert Brookings and also of Dr. Abraham Flexner brings a sense of contemporary reality to the achievements of Robert Brookings early in this century, which without their presence among us might seem to many of you only legendary history.

Let us recall that in 1895, Mr. Brookings had become President of the Corporation of Washington University, the new site for its campus was selected and a few of the new buildings were erected in time for use by the World's Fair in 1904. The Medical School had been reorganized and established on Locust Street and Jefferson Avenue.

In the fall of 1909 the University he had vitalized and rebuilt was in operation on the new campus. A new epoch in its history had begun. Mr. Brookings had abundant reason for pride in the splendid attainment of his dreams. We can imagine his feelings when he received one day a letter from an old friend, Henry S. Pritchett, president of the Carnegie Foundation for the Advancement of Teaching, transmitting a report by Dr. Abraham Flexner describing his inspection of the Medical School. He rated it as "entirely out of harmony with the rest of the university." "It must be either abolished or reorganized." "Heroic measures are necessary." (Phrases quoted from report.)

Naturally this indictment of his medical school offended Robert Brookings. He went at once to New York and protested vigorously. Dr. Flexner's reply was his offer to return to St. Louis and re-examine the school with Mr. Brookings—which they did. Flexner won the argument. In doing so he described vividly the unique opportunity to create in St. Louis a modern medical center, to serve not alone this community but to stand as an example for the West. Painted in those terms the challenge appealed to Robert Brookings. He became almost overnight an ardent pleader for the improvement of medical education. After winning the consent of his closest friends on the Board, especially W. K. Bixby and Edward Mallinckrodt, he decided to create an ideal medical center to add to "his" Washington University. He wasted no time.

By the spring of 1910 a group of new heads of departments had been selected with the advice of Dr. W. H. Welch, Dr. Simon Flexner and others:

negotiations for two new hospital affiliations were under way: Mr. Brookings had changed his will to insure financial support for the venture. In June of that year a group of "young wise men from the East" (as they were called by some) assembled in St. Louis to view the plans Mr. Brookings had ready—and each of us to make preparations for conducting courses to start three months later. In September the members of this group reported for duty and the second reorganization of the medical school had begun. It sounds incredible, but that is how it happened. The gracious welcome we received is a fond memory.

The enthusiasm and energy of Robert Brookings were infectious. To his type of idealism and devotion the young heads of departments were susceptible; faith in his visions was the reason they had accepted their posts. They learned from him and doubtless he learned from them. To be sure there were difficult periods; all was not smooth sailing. But I recall no instance when he did not support the considered opinion and recommendation of the executive faculty. That record has become a tradition of this institution, and is, I believe, one of its strengths. To this day the policies and ideals then established with the blessing of Robert Brookings remain the guiding principles of this medical center.

Five years later, in 1915 as many here will recall, the new buildings were dedicated by a three-day ceremony in which many noted men took part. At the first session Chancellor Hall presented the first speaker in these words: "the president of the Corporation, Robert Somers Brookings, the one man, preeminently, whose dream is this day realized." Mr. Brookings' first words were: "The published report of the Carnegie Foundation . . . on medical education in this country" . . . and other documents "have made medical education a very live issue in this country" . . . "and have arrived at a general understanding of what should constitute today an ideal plant and organization for the teaching of medicine and for medical research." "In the buildings we dedicate today and their affiliated hospitals Washington University has undertaken to produce a plant which we believe conforms to this ideal." His closing sentence reads: "We hope that our efforts will contribute to raising the standard of medical education in the West, and that we will add, through research activities, our fair quota to the sum of the world's knowledge of medicine." I wish he could be here today to hear and see the measure to which his hope has now been realized.

A fact worthy of record at this point is that all of the funds to erect and equip the plant dedicated that day in 1915 came from the generosity of citizens of St. Louis, the largest single donor being Robert S. Brookings. He gave personally the three laboratory and clinic buildings.

With the new medical school and hospitals in operation the need for additional financial support became urgent. I know because that year I became dean. Once again Dr. Abraham Flexner was a friend of this University. He had become an officer of the General Educa-

tion Board and had persuaded its trustees and Mr. Rockefeller to make available large sums to stimulate the improvement of medical education. The first time, you will recall, he gave advice only; now the need was money as well as counsel. Having acted on Dr. Flexner's advice, Mr. Brookings had good claim on a share of funds for endowment, which Johns Hopkins alone had then received.

I well recall going to New York with Mr. Brookings in the summer of 1915 to negotiate and collect the first installment of a large gift by the General Education Board for endowment of three clinical departments. Dr. Flexner and his chief, Dr. Wallace Buttrick, with the approval of their trustees, had promised a million dollars, two-thirds of the sum needed. W. K. Bixby, Edward Mallinckrodt and Mrs. Culver provided the balance. Just before leaving Dr. Flexner's office that afternoon Mr. Brookings received a check for a large sum as first payment on the gift—perhaps for a hundred thousand dollars or more. Going uptown on the elevated he mused aloud over the happy outcome, meanwhile rolling the check between his fingers as a boy would fondle a new toy. I remember suggesting that he put the paper in a safer place. That evening at the theatre he was in a jolly mood; the play was "Fair and Warmer."

That gift was the first of many this institution was to receive from the Rockefeller Foundation. Perhaps Dr. Gregg will tell us what the present officers think of their investments in Washington University.

The last time I talked with Mr. Brookings was in December, 1917. He had left St. Louis to become a member of the War Industries Board and was living in Washington, D. C. Although deeply engrossed in immense responsibilities, he invited me to dinner at his home and was interested as always in news about the medical school and as devoted to its welfare.

The last time I saw him was at the 1929 Commencement when he received *two* honorary degrees following his retirement from the Corporation. One degree was Doctor of Laws, the other Doctor of Medicine. Award of the honorary M.D. to a layman was the highest honor the medical faculty has ever given, and one he highly appreciated. A like compliment was paid him by physicians everywhere in refusing to accept from him any payment for service rendered. All knew of his great service to medicine.

In addition to his creative vision, his rare qualities of leadership and the capacity to achieve his goals, so evident in the life of Robert Brookings, he possessed another quality that impresses me as even more remarkable. He shunned personal credit or popular acclaim for his achievements; the service he rendered was for him its own reward.

At the time of the dedication of the Medical School in 1915, Governor Francis and others of the Corporation proposed that the school be named the Brookings School. Mr. Brookings discouraged and rejected that honor, believing it might deter later gifts from others, which he knew would be needed.

There is a phrase in his biography by

Hagedorn that expressed this trait in Mr. Brookings' character. The author relates the childhood experience when as a boy Robert went with his uncle Dr. Robert Carter, a country doctor, on his rounds to visit patients and was called by them "the little doctor." Hagedorn writes, "this influence clung to him as a sense, dimly perceived and inarticulate, that medicine mattered supremely, and that honorable living was the unostentatious giving of oneself."

That is the picture of Robert Brookings, as I remember him.

Recalling Some Events in the History of the Medical Fund Society

by Robert J. Terry, M.D.
Professor Emeritus of Anatomy
Washington University School of Medicine

My friend, the late Dr. John Blaisdel Shapleigh, has written the history of the Medical Fund Society compiled from the minutes of that organization, published in 1919. Without this faithful record the present address would probably not have been attempted. On this occasion, which seems an appropriate one, I want to recall some events in the life of the Society and to tell what progress has been made toward terminating the organization which had achieved its purpose many years ago. I welcome the opportunity to do this.

Dr. Charles Alexander Pope of Huntsville (originally Twickenham), Alabama, was Dean of the St. Louis Medical College when he died in 1870, and the school building which he owned, located on Seventh Street, was offered for sale. It was necessary for the faculty to continue to use the building. This was the circumstance that led to the origin of the Medical Fund Society, and the purchase of the property was the immediate object of its endeavor. The Society was formed by nine members of the faculty of the St. Louis Medical College, acting under the advice of a distinguished St. Louis lawyer. These founders were James Clemens, of the family of Missouri's Laureate, who lived but a year after his election to the Society; Abram Litton, John B. Johnson, Elisha H. Gregory, Elsworth F. Smith, L. Ch. Boisliniere, J. S. B. Alleyne, John T. Hodgen, inventor of the splint, and John J. McDowell, nephew of Dr. Daniel Drake, grandnephew of the ovariotomist.

The St. Louis Medical College had neither university affiliation nor endowment and, as in the case of most American medical schools at that time, was operated on the tuition fees of its students. When the college building was posted for sale an idealistic plan was evolved among those faculty members who formed the Medical Fund Society; namely, that of buying the

property themselves and of holding it in trust as an endowment for the promotion of medical education. This lofty objective was to be realized by the unique method of providing the funds necessary, from the lecture fees of the members of the Society. As stated by Dr. Gustav Baumgarten years later: "The unparalleled fact being that the permanent endowment of a school has come, not from the patronage of wealthy fellow-citizens, but from the devotion and self-sacrifice of its own corps of teachers."

With the acquisition of the title to the property, an additional source of revenue came in rent paid to the Society by the faculty of the St. Louis Medical College and later by the Missouri Dental College. As Dr. Shapleigh records, gifts were rarely received, citing only three, those of Mrs. Julie January, Mrs. Laura C. Hill, and Mr. Charles Rudolph.

Such an undertaking imposed heavy responsibilities upon the Society and required a form of organization that would operate properly in accordance with the laws. Quoting Dr. Shapleigh: "The legal matters pertaining to the purchase of the Seventh Street property and the incorporation of the Society had been placed in charge of Mr. Henry Hitchcock, and to them he had given a great deal of time and thought." The Articles of Association, issued March 9, 1872, committed the Society to holding its property as a sacred trust for the promotion of medical and surgical science. Regarding membership in the Society, the charter limited the personnel to physicians in medical faculties of St. Louis County. Dr. Hodgen and Dr. McDowell, it may be noted, had been on the faculty of the Missouri Medical College before the Civil War. When Mr. Hitchcock declined to charge for his services, the Society manifested its appreciation of his valuable assistance in a resolution establishing in 1872 the "Hitchcock Scholarship," giving Mr. Hitchcock the privilege of sending young men to the St. Louis Medical College whom he deemed deserving of assistance. Some of the beneficiaries of the Scholarship became leaders in their professions, as Dr. Shapleigh relates.

In time the Seventh Street building became unsuitable for the study of such a subject as medicine, that is constantly broadening its knowledge of disease by discoveries and the introduction of more precise methods; and, besides, the location had serious disadvantages for an educational institution. The property was sold and with the proceeds the Medical Fund Society bought a lot and in 1892 erected a new college building on Locust, just west of Eighteenth Street. The building was planned under the direction of a committee of the Society composed of Drs. John Green, Gustav Baumgarten, and Henry H. Mudd. The broad provisions of its charter permitted the Society to promote medical education in many ways and its contribution to a foundation in support of the annual Hodgen Lecture may be cited as one of the Society's uses of its privileges.

The School in 1892 was still called the St. Louis Medical College although its affiliation with Washington University had been established. When it was joined by the Missouri Medical College

in 1899, it was known by its official title, The Medical Department of Washington University. The union of these medical schools, the oldest in the West, picturesque in their rivalry, resulted in increased clinical and laboratory facilities and consequently better courses of instruction, the graduating of more carefully trained physicians. Entrance requirements were raised, full-time heads of the pre-clinical departments were appointed. Such evidence of progress caused the School to be more widely known and its spirit and objectives to receive wider recognition among medical educators. I recall with a thrill of pleasure listening, when a young man, to the scholarly valedictory address of Dr. Frederick Shattuck, and of my chief, Dr. Charles Minot, who saw a real opportunity for the development of a great school in a city that could boast the heritage and inspiring example of two illustrious investigators, both physicians — William Beaumont, the surgeon, and George Engelmann, the botanist. The School was visited by the leaders of the time, Osler, Jacobi, Welsh and by other less famous but gifted physicians and investigators who showed keen interest in the work of our mid-western medical college.

The School was benefited by its connection with the University in added dignity and security, for though the University contributed nothing for the operating expense of its Medical Department, it stood back of it financially. It continued to be self-supporting until 1910 when a reorganization of the faculty was brought about and the University assumed the financial obligations of its medical unit. Many of the old faculty remained and new blood was brought in with the group of young men trained in the East who entered enthusiastically into the problems of developing a university school of medicine with its complex structure and infinite relations.

In 1912 the Society transferred the title of the Locust Street property to Washington University. It had cost $130,000; there was a bonded debt of $70,000 which the University assumed, and generously cancelled the Society's indebtedness to the University. A great burden of responsibility was thereby lifted from the Society. Meeting payments on borrowed funds was sometimes a severe strain; in one instance, money was borrowed from the banks on the personal notes of members. In the transfer of title the Society presented to the University as a gift the scientific apparatus and laboratory furniture it owned at the time, its anatomical and pathological preparations and books. These were the nuclei of the teaching museums of our present departments of anatomy and pathology and of our imposing library collections.

When the great benefactor of Washington University Medical School, Robert Somers Brookings, decided to devote his genius and fortune to raising the Medical Department to the highest degree of usefulness, he had already gained by intensive study an amazingly broad and detailed knowledge of medical schools and medical educational methods. He traveled extensively in pursuit of information, became personally acquainted with medical edu-

cators, and learned from them at first hand the things he wanted to know. Of the founders of the Medical Fund Society Mr. Brookings knew Dr. Johnson and Dr. Gregory personally, and if not acquainted with those other charter members, Drs. Alleyne, Smith and Boisliniere who lived well into the 1890s, he must have known about them. Charles Nagel, the eminent jurist and statesman, had been a member of the Society for six years. Those in the Society at the period of the transfer of the Locust Street property were Dr. Washington E. Fischel, President; Dr. Frank Fry, Second Vice-President; Dr. John B. Shapleigh, Secretary; Dr. John Green, Treasurer; Dr. Henry Schwarz, Dr. Greenfield Sluder, Dr. Norman B. Carson.

In the negotiations that concerned property when the Missouri Medical College joined the St. Louis Medical College, the Society was an active participant. The older members of the two parent schools were among the leading physicians of St. Louis; nationally known and many of them officers in the national medical societies. Mr. Brookings knew all of these men and knew all that was of importance in the operation of the two schools. He must have learned of the altrustic and daring enterprise originated and carried to success by the Medical Fund Society. Can we doubt that this knowledge gave our benefactor encouragement to undertake his humanitarian project and increase his faith in its eventual success?

The Medical Fund Society realized the accomplishment of its objectives when the University assumed the financial obligations of the Medical Department, but its organization remained intact, meetings continued to be held, vacancies caused by resignation or death were filled by election of new members. Today the members are five: Dr. Vilray Papin Blair, Dr. Walter Fischel, first vice-president; Dr. Otto Schwarz, second vice-president, Dr. Walter Baumgarten, Jr., secretary-treasurer; Dr. Robert J. Terry, president. Certain assets have been held by the Society in the form of shares of stock and cash in banks. What useful thing could be done with these assets within the intent of the charter? The Society considered the question and decided to transfer the value of the shares of stock, amounting to sixty-five hundred dollars, to Washington University, to be held as an endowment for two Medical Fund Society Prizes, one in Medicine, one in Surgery, for annual award to two senior students of the Medical School who excelled in the subjects named. The University has accepted the funds under the conditions specified and the Prizes are now established. Legal steps are in progress to terminate the Society; residue cash in banks has been offered to the University as an addition to the Prize endowment. The book of the Society's minutes will be presented to the Medical School to be jealously guarded among its most precious archives; and the Secretary's correspondence will be placed where it can be consulted, in the possession of the

(Concluded on page 133)

Proceedings of the Washington University Medical Society

The March 15 meeting of the Washington University Medical Society presented a symposium on certain aspects of adrenal cortical function, and attracted a crowd of students and faculty members which filled the Medical School Auditorium. Dr. Gustave J. Dammin presided and the program was arranged by Dr. Albert I. Mendeloff. Abstracts of the papers follow:

URINARY ADRENAL METABOLITES: A CLINICAL INDEX OF ADRENAL CORTICAL ACTIVITY

by William H. Daughaday, M.D.
Department of Biological Chemistry

In diagnosing disease of the adrenal or following the response of patients with ACTH (adrenocorticotrophic hormone) treament, the measurement of adrenal hormones and their products in the urine has proved useful. Methods have been developed by a number of workers during the past ten years which measure such substances by either a biological assay using adrenalectomized mice or by certain chemical properties. One such chemical method has been used at Barnes Hospital for two years. The urine of patients with adrenal insufficiency have decreased amounts of adrenal substances; greatly increased amounts are found in adrenal hyperactivity (Cushing's syndrome), postoperatively and in late pregnancy. ACTH used in treating rheumatoid arthritis caused a great increase in these substances. Although the adrenals are important in maintaining normal salt metabolism, during salt restriction there is no evidence of increased adrenal secretion as measured by existing tests.

METABOLIC EFFECTS OF ACTH

by Ethel Ronzoni, Ph.D.; Samuel Trufant, M.D.; Edwin F. Gildea, M.D.; and Miss Marlene Hunter
Department of Neuropsychiatry

Balance studies were made on five psychotic patients before and during treatment for from 5 to 26 days with ACTH. All the patients had normally responsive pituitaries and adrenals as shown by the decrease in circulating eosinophiles and lymphocytes after a test dose of Epinephrine. A single dose of ACTH, 25 mgs., produced prompt fall in circulating lymphocytes and eosinophiles. They all had normal glucose tolerance and were normally sensitive to insulin before the hormone was given.

While there were individual variations in the quantitative response to the

hormone, qualitatively the response showed ACTH to cause all of the known activities of the adrenal cortical hormones. Desoxycorticosterone-like activity was shown by marked retention of sodium and water. One patient on 100 mgs. of the hormone showed fluctuations in sodium retention but when given 150 mgs. showed and sustained retention of both sodium and water. The well-known effect of the 11 - 17 oxygenated corticoids on protein and carbohydrate metabolism was also evident. All patients showed a negative hormone treatment amounting to from 3 to 6 grams a day. The patient receiving 150 mg. of hormone excreted 16 to 20 gms. of sugar a day. The reduction of lymphocytes and eosinophiles in the circulating blood is also evidence of production of the 11-17 oxygenated steroids.

Investigation of the excretion of steroids showed an increase of 17 ketosteroids with a particularly good increase in one having the properties of dehydroisoandrosterone. The increased excretion in these steroids varied from 20 to 50 mg. per day. There was also an increase in the corticoids having a ketol side chain. As measured by the reducing power the increase was equivalent to 3 to 10 mg. of 17-OH cortisterone per day. There is also a marked increase in steroids conjugated with glucuronic acid. The nature of the steroid has not yet been identified.

The five patients to whom we have administered ACTH in various doses have all been psychotic. Although no conclusions as to the value of ACTH in such states can be drawn from this material, two patients showed improvement coincident with its administration. This has been maintained to date. Two other patients experienced an increase in their sense of well-being and appearance during the period of administration but reverted to their previous state on withdrawal. The fifth patient showed no clinical change while receiving the hormone or afterward.

CHANGES IN BLOOD EOSINOPHILS AS AFFECTED BY OPERATION AND ANESTHESIA

by Arthur H. Stein, M.D., Willard Walker, M.D., and Robert Elman, M.D.

Department of Surgery

The variation in circulating eosinophils as an index of adrenal cortical activity was studied in a group of thirty-five surgical patients in the Barnes Hospital. The technic used in counting the cells was that described by Randolph in 1944. This consisted of using a diluting fluid of equal parts of 0.1 per cent methylene blue in propylene glycol and 0.1 per cent phloxine in propylene glycol. The count was then done in a Fuchs-Rosenthal chamber.

Patients were selected at random on the surgical wards, and at the termination of the study the majority of cases fell into the following groups:

GROUP I. This group consisted of six patients undergoing cholecystectomy,

two gastric resection, five abdominoperineal resection, one hip disarticulation, one small bowel resection, one appendectomy, and three thyroidectomy, all done under general anesthesia (gas-oxygen-ether). In all there was a fall of the total circulating eosinophils from the normal (100-300/cu.mm.) to near zero or zero within a period of four to six hours following surgery. The counts remained down for a period of two to three days and then gradually returned to the normal levels.

GROUP II. This group consisted of five patients undergoing herniorrhaphy under spinal anesthesia, one herniorrhaphy under local anesthesia, three lumber sympathectomy under spinal anesthesia, and five transurethral prostatic resection under pentothal and nitrous oxide anesthesia. These patients did not show the typical fall in eosinophil count observed in Group I. Instead the following changes were noted:

(1) After herniorrhaphy under spinal anesthesia a significant decrease in eosinophils occurred, but it was not as pronounced as in Group I.

(2) After lumbar sympathectomy under spinal anesthesia a slight, but questionably significant decrease occurred.

(3) After transurethral resection the response varied, some showing a fall in eosinophils and others remaining at essentially the normal level.

(4) One herniorrhaphy under local anesthesia showed no decrease in circulating eosinophils.

It should be emphasized that all patients in this group received as part of the anesthetic procedure injections of ephedrine or adrenalin. The latter itself is known to lead to a fall in eosinophils. Had these drugs not been used, it is likely that the eosinophil response would have been even less evident.

It seems clear from these observations that a fall to zero in the eosinophil count does not always occur after surgical trauma. Because the failure of patients to show this effect was observed after operations done under spinal and local anesthesia suggests that the integrity of the nerve pathway from the area of trauma plays an important part in the pituitary adrenal reaction, as revealed by the eosinophil response. Failure to show the characteristic response to patients undergoing transurethral resection under pentothal nitrous oxygen anesthesia also suggests that significant trauma is an important factor. The findings indicate, moreover, that failure to observe an eosinophil response following operation does not necessarily mean that there is an adrenal cortical insufficiency. For such a diagnosis it is likely that a specific test with ACTH or possibly adrenalin will be required. Work along this direction is now in progress.

Medical Fund Society (Cont.)

Missouri Historical Society.

It is the hope of the present members of the Medical Fund Society that the actions taken looking to the termination of the organization would have been approved by its Founders.

CLINICAL IMPLICATIONS OF RECENT STUDIES WITH ACTH AND CORTISONE

Cyril M. MacBryde, M.D.
Department of Internal Medicine

Recent studies with two hormones—one from the pituitary and one from the adrenal cortex—have given evidence of the opening of a new vista in medicine, both in the understanding of and in the treatment of a wide variety of diseases. For years clues have accumulated, suggesting that the pituitary-adrenal cortex system is important in reaction to stress and in mobilization of defense mechanisms. Selye suggested several years ago that the "alarm reaction," which may be induced by a number of stresses, is manifested largely through extreme pituitary-adrenal participation and that rheumatic fever, rheumatoid arthritis, nephrosclerosis and other conditions may be "diseases of adaptation" resulting from abnormal pituitary-adrenal adaptative activity.

The metabolic effects of ACTH therapy seem to be agreed upon in general. Urinary corticoid and 17-ketosteroid excretion increases, as does urinary uric acid and potassium. Sodium excretion diminishes, and with salt and water retention there may be considerable weight gain. Nitrogen excretion may be normal or somewhat increased. The blood sugar may be elevated and glycosuria may occur in some patients receiving continued large doses. When treatment is prolonged and excessive amounts of ACTH or cortisone have been used, symptoms have been produced which suggest Cushing's syndrome.

Hematologic changes may be striking. There occurs a marked fall in the circulating eosinophils, a drop in lymphocytes, and a rise in the neutrophils.

Cortisone, the adrenal cortex hormone ("compound E") produces in general the same metabolic effects as those produced by ACTH. This is to be expected, of course, since ACTH acts by stimulating the adrenal cortex; however ACTH causes increased secretion of several adrenal hormones, including the androgens, and it may act chiefly in augmenting production of "compound F" rather than of "compound E."

In the Metabolism Division during the past 2 years Dr. William Daughday, Dr. Bernard Sweeney and I have studied a number of aspects of the various problems discussed tonight. We have been unable to inhibit the pituitary's output of ACTH by giving DCA (desoxycorticosterone acetate). By extreme variations in sodium intake we have been unable to alter urinary cortin and 17 ks levels. It would be useful, if possible, to find a way to *diminish* ACTH production in certain clinical states (Cushing's syndrome, acromegaly).

We have found that fever therapy, formerly as popular and exciting as ACTH and cortisone are now, probably acts at least partly through the same mechanisms in mobilizing defense responses. Other stress conditions seem to act similarly: during pneumonia one patient was temporarily cured of severe

chronic asthma; another had complete but brief remission of rheumatoid arthritis following appendectomy.

Among the reactions which may be caused by the excessive use of ACTH or cortisone are: interference with wound healing; abnormal carbohydrate and nitrogen metabolism (Cushing's-like); salt and water retention (dangerous increasing edema in cardiac disease); muscular weakness, potassium loss, low serum K. Therefore these hormones must be used with caution, and careful observation for untoward effects is necessary.

Other methods to regulate the hypothalamus (which governs to a large extent pituitary activity and ACTH production) may be found—fever, trauma, various stresses, adrenalin, etc., and their influences are being studied.

Other steroid hormones, similar to cortisone in chemical structure, may prove to have some of the desirable therapeutic properties, but we hope fewer potential dangers.

Two Indian Students Doing Research Here

Miss K. Padmasini Ayengar and Dr. Jyotirmoy Chatterjee, both fellows in cancer research from India, are the most recent additions to the staff in cancer research.

Miss Ayengar, or Padma as she is called by her associates, arrived in St. Louis the latter part of December. She came here from the Tata Memorial Hospital in Bombay, and previously was with the Indian Institute of Science. She graduated from the University of Travancore with a B.S. degree in 1944. Her work is primarily the study of the cytochemistry of tissues in various phases of growth.

Dr. Chatterjee came here from the Indian Institute for Medical Research in Calcutta, arriving on January 28. He was graduated from the University of Calcutta in 1948 with a degree of bachelor of medicine, equivalent to a doctor's degree in this country. Dr. Chatterjee's study is on the surface of malignant and normal cells with the phase microscope.

Four Senior Students Receive Gift Subscriptions to Medical Journal

Four students in the senior class have been selected to receive one-year gift subscriptions to the *Journal of the History of Medicine and Allied Sciences* from Mrs. Josiah C. Trent in memory of her late husband, Dr. Trent, of Durham, N. C. The students are: Seymour Advocate of Brooklyn, New York; Elmer B. Brown, Jr., of St. Louis; Frank A. Howard, from Enid, Okla.; and J. Max Rukes, of Rosedale, Ind.

Dr. Farber of Harvard Lectures

A special lecture was presented by Dr. Sidney Farber, professor of pathology at Harvard Medical School and director of cancer research at Children's Hospital Medical Center in Boston, at the School of Medicine on February 20. Dr. Farber termed the future for chemical treatment of cancer as "encouraging," and reported that knowledge of the treatment of cancer is 50 per cent greater today than it was ten years ago. His topic was "Malignant Tumors in Childhood."

Report on Dormitory Center Campaign

Our list of contributors has grown longer, and the total amount pledged has reached the sum of $48,932.10. Of this amount, $30,611.42 has been collected, and the remainder is to be paid within the next two years.

We have almost reached the $50,000 mark, and our immediate goal is the first $100,000. With that amount in hand, we would be able to start negotiations leading to action on the building program, beginning with one wing of the proposed Dormitory Center.

A further report of the campaign was made at the Medical School Alumni Reunion on May 5 and 6.

The following list shows those who have already made contributions or pledges.

Samuel B. Grant, Chairman

Medical Student Dormitory Fund Contributors from Each Class

1949—Living Graduates, 95
Eugene W. Pearce, Washington, D. C.

1948—Living Graduates, 90
Walter A. Fernau, Jr., Cincinnati, O.
David A. Guterman, Elgin, Ill.
Juro J. Shintani, Perry Point, Md.

1947—Living Graduates, 96
Charles G. Clay, Rantoul, Ill.
Marvin Cornblath, St. Louis
William C. Dunckel, Charlottesville, Va.
Helen Hofsommer Glaser, St. Louis
Burnet W. Peden, St. Louis
Virginia H. Peden, St. Louis

1946—Living Graduates, 91
James W. Owen, Jr., Skiatook, Okla.
Frank Vellios, St. Louis
Leonard J. Wiedershine, Aurora, Colo.

1945—Living Graduates, 97
John T. Farrar, Boston, Mass.
Samuel B. Guze, Newington, Conn.
John T. Johnstone, Jr., St. Louis
Ceylon S. Lewis, Jr., Salt Lake City
Roscoe Maxwell, Punta Gorda, Fla.
Eugene E. Taylor, Mocksville, N. C.
Gary B. Wood, St. Louis

1944—Living Graduates, 99
Rowe F. Bisbee, Ada, Okla.
Albert B. Eisenstein, St. Louis
J. K. Frost, Centralia, Ill.
Ervan Levine, Vandalia, Mo.
Clayton H. Manry, Syracuse, N. Y.
Francis E. Pennington, St. Louis
David E. Smith, St. Louis

1943 (Dec.)—Living Graduates, 112
John F. Blinn, Jr., Stockton, Calif.
C. Read Boles, St. Louis
William P. Callahan, Wichita, Kan.
Terrell Covington, Jr., McKinney, Tex.
Mary Jordan, Ridley Park, Pa.
Edward H. Kowert, St. Louis
Elaine K. Lince, Pasadena, Calif.
Torrence A. Makley, Jr., Columbus, O.
Walter A. Rohlfing, Fresno, Calif.
Tom G. Stauffer, Scarsdale, N. Y.
Herbert C. Wiegand, St. Louis
Frances C. Wilson, Tampa, Fla.

1943 (March)—Living Graduates, 95
Grace E. Bergner, St. Louis
Raymond M. Charnas, St. Louis
Harlan I. Firminger, Bethesda, Md.
Melvin L. Goldman, St. Louis
Ira W. Liebner, Brooklyn, N. Y.
Eichi Masunaga, T. H.
Roberts B. Pappenfort, New York, N. Y.
Ernest S. Rogers, San Francisco, Calif.
Carvel T. Shaw, Hermann, Mo.
David A. Stadtner, Stockton, Calif.

1942—Living Graduates, 93
William M. Anderson, Richmond, Va.
French H. McCain, Birmingham, Mich.
William G. Reese, Perry Point, Md.
Herman Rice, Temple, Tex.
Frank O. Shobe, St. Louis
George L. Watkins, Farmington, Mo.

1941—Living Graduates, 93
Robert J. Cook, St. Louis

Peter O. Fleming, Topeka, Kan.
Anne T. Goetsch, Berkeley, Calif.
Samuel W. Gollub, St. Louis
Geo. Bruce Lemmon, Springfield, Mo.
Harold E. McCann, E. St. Louis
V. A. Mueller, Wichita, Kan.
C. A. Nielsen, Seattle, Wash.
Joseph W. Noah, St. Louis
Carol H. Rehm, Los Angeles, Calif.
William L. Topp, Seattle, Wash.

1940—Living Graduates, 90
Donald S. Bottom, Alton, Ill.
Seymour Brown, St. Louis
Russell J. Crider, St. Charles, Mo.
Roland R. Cross, Hines, Ill.
L. R. Fernandez, Laupahoehoe, T. H.
James M. Foerster, Wausau, Wis.
Otto H. Grunow, St. Louis
Robert E. Koch, St. Louis
James Mann, Boston, Mass.
Gordon F. Moore, Alton, Ill.
Charles G. Obermeyer, St. Louis
Willard R. Rowland, Portland, Ore.
Llewellyn Sale, Jr., St. Louis
John S. Skinner, St. Louis
Robert M. Smith, St. Louis

1939—Living Graduates, 96
Alfred K. Baur, St. Louis
Irving L. Berger, Cleveland, Ohio
Vilray P. Blair, Jr., St. Louis
Heinz E. Cron, San Francisco, Calif.
Benjamin Milder, St. Louis
Edward H. Reinhard, St. Louis
Minton D. Ritter, Margate City, N. J.
Gerald A. Slusser, Silver City, N. Mex.
O. W. Towers, St. Charles, Mo.

1938—Living Graduates, 93
Lawrence M. Kotner, St. Louis
Robert G. Moles, Hanford, Calif.
Anthony Piraino, Oberlin, Ohio
Philip Rosenblatt, New York, N. Y.
Roy W. Thomas, Redding, Calif.

1937—Living Graduates, 93
Samuel Brady, Gary, Ind.
G. L. Calvy, Cleveland, Ohio
Martin A. Compton, Richmond, Va.
John R. Connell, Denver, Colo.
J. A. Fiorito, New Haven, Conn.
William H. Gray, Yakima, Wash.
Robert C. Kingsland, St. Louis
Carl E. Lischer, St. Louis
Edgar H. Little, New Orleans, La.
Elizabeth Lowenhaupt, San Francisco
Ralph C. Petersen, Glendale, Calif.
Charles M. Polan, Huntington, W. Va.
Henry N. Reid, Rome, N. Y.
Lloyd Rosenbaum, Anderson, Ind.
H. L. Townsend, Louisville, Ky.
David R. Wall, Wichita, Kan.
Marie H. Wittler, Wheaton, Ill.

1936—Living Graduates, 95
James H. Bryan, St. Louis
F. R. Crouch, Farmington, Mo.
Norman W. Drey, St. Louis
Stephen Ellis, Coffeyville, Kan.
John L. Horner, St. Louis
W. H. Jacobson, Canton, Ohio
Nathan R. Kahn, Brooklyn, N. Y.
Frank McDowell, St. Louis
James D. Morrison, Billings, Mont.
R. A. Nussbaum, St. Louis
Samuel Schneider, St. Louis
Warren B. West, Ogden, Utah
Robert A. Wise, Houston, Tex.

1935—Living Graduates, 89
I. J. Flance, St. Louis
Alfred W. Harris, Dallas, Tex.
A. Herman Hutto, St. Louis
Norman M. Johnson, Clarinda, Iowa
Bruce Kenamore, St. Louis
Ellen S. Loeffel, St. Louis
Edward Massie, St. Louis
Sidney Messer, Venice, Calif.
Clark G. Porter, Three Rivers, Mich.
Laurence G. Pray, Fargo, N. D.
David Rothman, St. Louis
Bernard Schwartzman, St. Louis
Ben H. Senturia, St. Louis
A. J. Steiner, St. Louis
Irvin Weisman, Granite City, Ill.

1934—Living Graduates, 88
Helen M. Aff, St. Louis
James M. Baker, Columbia, Mo.
Eugene M. Bricker, St. Louis
T. C. Campbell, New Orleans, La.
David Friedman, Granite City, Ill.
Paul O. Hagemann, St. Louis
Stanley Hampton, St. Louis
Louis G. Jekel, Phoenix, Ariz.
Dorothy J. Jones, St. Louis

Morris D. Marcus, St. Louis
M. Norman Orgel, St. Louis
H. D. Rosenbaum, St. Louis
John A. Saxton, St. Louis
Edna Schrick, Holland, Mich.

1933—Living Graduates, 88
Henry C. Allen, St. Louis
James W. Bagby, St. Louis
Russell J. Blattner, Houston, Tex.
Cecil M. Charles, St. Louis
Truman G. Drake, St. Louis
Wallace D. English, Cardwell, Mo.
C. A. Good, Rochester, Minn.
Carl G. Harford, St. Louis
John R. Haslem, Terre Haute, Ind.
W. W. Herman, Cleveland, Ohio
Joseph C. Jaudon, St. Louis
F. Craig Johnson, Denver, Colo.
A. A. Loverde, Chicago, Ill.
Alvin R. Miller, Seattle, Wash.
Lyman K. Richardson, New Orleans, La.
Richard Y. Sakimoto, Honolulu, T. H.
Robert T. Terry, Nashville, Tenn.
Oreon K. Timm, Danville, Ill.
R. M. Van Matre, Oklahoma City, Okla.
Wirt A. Warren, Wichita, Kan.
Lawrence M. Wilson, Olympia, Wash.

1932—Living Graduates, 84
Sim F. Beam, St. Louis
Brian B. Blades, Washington, D. C.
Louis T. Byars, St. Louis
B. S. Clark, Spearfish, S. D.
William Ehrlich, Newark, N. J.
Leo Gottlieb, St. Louis
Kiyoshi Inouye, Honolulu, T. H.
William H. Meinberg, St. Louis
Carl V. Moore, St. Louis
Paul B. Nutter, Spokane, Wash.
Sydney S. Pearl, Elizabeth, N. J.
C. O'Neil Rich, Salt Lake City, Utah
Wendell G. Scott, St. Louis
Barrett L. Taussig, St. Louis
Dwight H. Trowbridge, Fresno, Calif.
Sam R. Wallis, Kauai, T. H.
Helman C. Wasserman, St. Louis

1931—Living Graduates, 73
Delevan Calkins, St. Louis
Joseph Cieri, Piedmont, Calif.
A. W. Hankwitz, Milwaukee, Wis.
W. E. Keiter, Kinston, N. Car.
Mary Louise Newman, Jacksonville, Ill.
H. R. McCarroll, St. Louis
Robert F. Monroe, Louisville, Ky.
John A. Schindler, Monroe, Wis.

1930—Living Graduates, 74
Harold S. Bowman, Wichita, Kan.
M. A. Brennecke, Waimea, Kauai, T. H.
M. A. Diehr, St. Louis
Donald E. Eggleston, Macon, Mo.
Herbert H. Gass, India
Joseph J. Gitt, St. Louis
Alfred H. Hathcock, Fayetteville, Ark.
I. D. Newmark, Chester, Ill.

1929—Living Graduates, 72
A. W. Freshman, Denver, Colo.
Guerdan Hardy, St. Louis
Craig B. Johnston, Philadelphia, Pa.
Louis Kovitz, Kansas City, Mo.
Sidney Pakula, Kansas City, Mo.
Frank B. Queen, Portland, Ore.
Jay Marvin Salzman, Springfield, Ill.
A. Ford Wolf, Temple, Tex.

1928—Living Graduates, 63
A. N. Arneson, St. Louis
Edward Burns, Toledo, Ohio
Justin J. Cordonnier, St. Louis
H. R. Hildreth, St. Louis
Laurence L. Howard, Great Falls, Mont.
J. Ted Jean, St. Louis
R. D. Kepner, Honolulu, T. H.
Guy N. Magness, St. Louis
L. A. Malone, Terre Haute, Ind.
Earl L. Mills, Wichita, Kan.
John F. Patton, St. Louis
A. Victor Reese, St. Louis
Paul R. Rollins, Seattle, Wash.
Verne Ross, Stockton, Calif.
W. A. Ruch, Memphis, Tenn.
David M. Skiling, St. Louis
S. D. Soule, St. Louis
A. Lloyd Stockwell, Kansas City, Mo.
Jacob Stolar, St. Louis
Vincent T. Williams, Kansas City, Mo.
George H. Wood, Carthage, Mo.

1927—Living Graduates, 72
Everett C. Drash, Charlottesville, Va.
A. C. Fortney, Fargo, N.D.
Alfred G. Henrich, Los Angles, Calif.
Alfred J. Metscher, Enid, Okla.
W. R. Merrell, Brigham City, Utah

Kazuo Miyamoto, Honolulu, T. H.
Eugene O. Parsons, Kansas City, Mo.
Willard C. Schwartz, Manhattan, Kan.
Abigail E. Smith, Lexington, Mass.
Frances H. Stewart, St. Louis
Richard T. Taylor, Los Angeles, Calif.
Louis L. Tureen, St. Louis
Franklin Walton, St. Louis
W. B. Wilcoxen, Bowling Green, Mo.

1926—Living Graduates, 73
Reno A. Ahlvin, Kankakee, Ill.
James L. Benepe, St Paul, Minn.
H. M. Chandler, Waipahu, T. H.
Eric A. Cunningham, Louisiana, Mo.
Max Deutch, St. Louis
William B. Kountz, St. Louis
G. Wendell Olson, Fullerton, Calif.
Henry A. Romberg, Oshkosh, Wis.
J. C. Schmidtke, Elgin, Ill.
E. H. Theis, Granite City, Ill.

1925—Living Graduates, 69
George P. Bailey, Lakewood, Colo.
Robert J. Crossen, St. Louis
H. M. Denny, Union, Mo.
James J. Donohue, E. St. Louis, Ill.
B. Y. Glassberg, St. Louis
A. E. Hiebert, Wichita, Kan.
Richard K. Kimmel, St. Louis
Jerome S. Levy, Little Rock, Ark.
Joseph Magidson, St. Louis
Carl H. Matthey, Davenport, Iowa
Sam J. Roberts, Miami, Fla.
Melvin A. Roblee, St. Louis
Roland A. Slater, Peoria, Ill.
Gershom J. Thompson, Rochester, Minn.

1924—Living Graduates, 69
Alfred O. Adams, Spokane, Wash.
Roy F. Baskett, Texarkana, Tex.
J. William Beckmann, New York, N.Y.
Charles Drabkin, Los Angeles, Calif.
Perry E. Duncan, Springfield, Ill.
William B. Gnagi, Monroe, Wis.
Louis H. Jorstad, St. Louis
Elizabeth E. Koppenaal, Elmhurst, Ill.
O. Earl Whitsell, St. Joseph, Mo.

1923—Living Graduates, 50
Oliver Abel, Jr., St. Louis
William G. Becke, St. Louis
William L. Bradford, Rochester, N. Y.
James Barrett Brown, St. Louis
Walter J. Decker, Westfield, Pa.
George V. Feist, Kansas City, Mo.
Ben D. Senturia, Chicago, Ill.
Charles Teel, Bellingham, Wash.
J. Wm. Thompson, St. Louis
Clair O. Vingom, Madison, Wis.

1922—Living Graduates, 44
Calvin Clay, St. Charles, Mo.
James B. Costen, St. Louis
F. E. Sultzman, Hannibal, Mo.

1921—Living Graduates, 43
Lester J. Evans, Jackson Heights, N. Y.
J. C. McKitterick, Burlington, Iowa
Oscar C. Zink, St. Louis

1920—Living Graduates, 39
Robert L. Andrae, Louisiana, Mo.
Clifton H. Briggs, Pasadena, Calif.
Warren H. Cole, Chicago, Ill.
Alfred Goldman, St. Louis
Samuel B. Grant, St. Louis
Guy H. Hopkins, Pueblo, Colo.
William A. Hudson, Detroit, Mich.
Frederick E. Jostes, St. Louis
P. H. Kennedy, Hubbard, Ohio
Herman M. Meyer, St. Louis
L. J. Owen, Lincoln, Neb.
H. W. Wellmerling, Bloomington, Ill.
Harvey Lester White, St. Louis

1919—Living Graduates, 45
Duff S. Allen, St. Louis
Howard H. Heuston, Boulder, Colo.
Carl O. Kohlbry, Duluth, Minn.
E. H. Munro, Grand Junction, Colo.
Howard A. Plank, New York, N. Y.
A. B. Raffl, Syracuse, N. Y.
R. P. Roantree, Elko, Nev.

1918—Living Graduates, 26
Glover H. Copher, St. Louis
Wilbur G. Gillett, Wichita, Kan.
Elmer N. Liljedahl, Hollywood, Calif.
Arthur G. Mahle, Chicago, Ill.
O. Sundwall, Murray, Utah.
J. F. Pessel, Trenton, N. J.

1917—Living Graduates, 25
Archie A. Skemp, La Crosse, Wis.
J. E. Wattenberg, Cortland, N. Y.

1916—Living Graduates, 13
Earl C. Sage, Omaha, Neb.
Ray T. Woolsey, Salt Lake City, Utah.

1915—Living Graduates, 22
D. K. Rose, St. Louis

1914—Living Graduates, 8
John T. McLarney, Brookfield, Mo.

1913—Living Graduates, 20
F. O. Kettelkamp, Colorado Springs, Colo.

1912—Living Graduates, 30
Edwin C. Ernst, St. Louis
George S. Gilpin, Cleveland, O.
Wells C. Reid, Goodrich, Mich.
George L. Watkins, Farmington, Mo.

1911—Living Graduates, 22
Charles H. Hecker, Palo Alto, Calif.

1910—Living Graduates, 40
Stanley S. Burns, St. Louis
Frederic Hagler, Springfield, Mass.
John P. Keim, St. Louis
Peter G. Moskop, St. Louis
Claude D. Pickrell, St. Louis
Frederick O. Schwartz, St. Louis

1909—Living Graduates, 30
Carey B. Elliott, Raton, N. Mex.
W. N. Pugh, Salt Lake City, Utah

1908—Living Graduates, 31
W. A. Olds, Colville, Wash.

1907—Living Graduates, 28
C. C. Nash, Dallas, Tex.
Llewellyn Sale, St. Louis

1906—Living Graduates, 35
Martin J. Glaser, St. Louis
Arthur Gundlach, St. Louis
S. P. Martin, East Prairie, Mo.
S. B. McPheeters, Goldsboro, N. C.

1905—Living Graduates, 12
Jerome E. Cook, St. Louis
Walter Fischel, St. Louis
J. M. James, Henning, Ill.

1904—Living Graduates, 33
Paul Baldwin, Kennett, Mo.
N. M. Freund, St. Louis

1903—Living Graduates, 22
A. H. Myerdick, Mt. Pleasant, Iowa
Clive D. Scott, Louisiana, Mo.

1902—Living Graduates, 22

1901—Living Graduates, 20
Walter C. G. Kirchner, St. Louis
M. K. Wylder, Albuquerque, N. Mex.

1900—Living Graduates, 2

1899—Living Graduates, 41
C. L. Lawless, Marshall, Mo.
R. O. Raymond, Flagstaff, Ariz.
Selden Spencer, St. Louis
Julian B. Woodson, Lowesville, Va.

1898—Living Graduates, 30
J. G. W. Fischer, Alma, Mo.
R. B. H. Gradwohl, St. Louis
John Q. Roane, Carlyle, Ill.

1897—Living Graduates, 34
Theodore Greiner, St. Louis
Frederick E. Woodruff, St. Louis

1896—Living Graduates, 30

1895—Living Graduates, 27
H. A. Geitz, Monterrey, N. L., Mexico
Robert J. Terry, St. Louis

1894—Living Graduates, 14

1893—Living Graduates, 17
Andrew Darling, St. Louis
R. Clarence Stephens, Plymouth, Ind.

1892—Living Graduates, 4

1891—Living Graduates, 21

1890—Living Graduates, 6

1889—Living Graduates, 13

1888—Living Graduates, 15

1887—Living Graduates, 6

1886—Living Graduates, 4

1885—Living Graduates, 8

1884—Living Graduates, 8

1883—Living Graduates, 12

1882—Living Graduates, 1

1881—Living Graduates, 2
James A. Dickson, St. Louis
Willis Hall, St. Louis

1880—Living Graduates, 2

Other Donors

Mrs. T. R. Akin, Clayton, Mo.
Harry L. Alexander, M.D., St. Louis
Robert W. Bartlett, M.D., St. Louis
Leon Bromberg, M.D., St. Louis
J. J. Bronfenbrenner, Ph.D., St. Louis
Martin M. Calodney, M.D., St. Louis
Benjamin H. Charles, M.D., St. Louis
Gustave J. Dammin, M.D., St. Louis
Hallowell Davis, M.D., St. Louis

Joseph C. Edwards, M.D., St. Louis
Robert Elman, M.D., St. Louis
Ben Eiseman, M.D., St. Louis
Robert J. Glaser, M.D., St. Louis
Paul E. Kubitschek, M.D., St. Louis
G. E. Gruenfeld, M.D., St. Louis
Miss Helen D. Harkness, St. Louis
John Esben Kirk, M.D., St. Louis
Grover Liese, M.D., St. Louis
Robert G. Loeffel, St. Louis
Sedgwick Mead, M.D., St. Louis
Ivan N. Mensh, Ph.D., St. Louis
William H. Olmsted, M.D., St. Louis
Joseph C. Peden, Sr., M.D., St. Louis
Lawrence T. Post, M.D., St. Louis
M. Hayward Post, M.D., St. Louis
Herman J. Rosenfeld, M.D., St. Louis
Theodore B. Rosenthal, Ph.D., St. Louis
Harold Scheff, M.D., St. Louis
Arthur E. Strauss, M.D., St. Louis
Carl R. Wegner, M.D., St. Louis
Park J. White, M.D., St. Louis

Special Speakers at Cancer Conference in February

Dr. F. W. Spiers of the Radiotherapy Centre, Leeds, England, and Dr. Jesse P. Greenstein of the National Cancer Institute in Bethesda, Md., presented the topics for discussion at the cancer research conference in the Medical School on February 27. Dr. William B. Seaman led discussion following Dr. Spiers' presentation of "Physical Aspects of High Voltage Radiotherapy," while Dr. Christopher Carruthers was in charge following Dr. Greenstein's talk on "Neoplastic Transformation as a Biological Fractionation of Related Enzyme Systems." These cancer conferences are held once a month.

A. M. A. Leader Speaks at Alumni Dinner

The Alumni Association was privileged to have as its guest speaker for the 1950 Clinical Reunion on May 5 and 6, Dr. Ernest E. Irons, president of the American Medical Association.

Dr. Irons, who is also clinical professor of medicine emeritus at the University of Illinois School of Medicine, spoke on "The Practice of Medicine." He has practiced medicine in Chicago since 1903, when he was graduated from Rush Medical College. He holds the Ph.D. degree from the University of Chicago.

The Annual Dinner was held Friday evening, May 5, in the Gold Room of the Hotel Jefferson at 7:00 P. M.

The scientific program starting at 9:30 a. m., Friday, had five alumni as speakers. They were Dr. Dalton K. Rose '15, president of the Medical Alumni Association; Dr. Harvey Lester White '20, professor of physiology; Dr. Erwin R. Schmidt '16, professor of surgery at the University of Wisconsin; Dr. Gershom J. Thompson '25, professor of urology at the University of Minnesota and head of the Section on Urology at the Mayo Clinic; and Dr. Paul S. Barker, '20, professor of internal medicine at the University of Michigan.

Other W. U. staff members who spoke were: Drs. Robert A. Moore, Harry L. Alexander, Edmund V. Cowdry, Jean V. Cooke, J. Albert Key, and Lawrence T. Post.

Clinics in operative surgery, internal medicine, obstetrics-gynecology, pediatrics, and a tumor conference were presented on Saturday morning.

DEPARTMENTAL NEWS

Anatomy

Dr. Ernest Gardner, who was instructor in anatomy here in 1941-42, was appointed visiting associate professor of anatomy for six weeks beginning January 30. On the day of his last lecture, freshmen anatomy students presented him with an engraved cigaret lighter as a token of their appreciation. He is now assistant professor of anatomy at Wayne University College of Medicine, Detroit, Mich.

Dr. Mildred Trotter, professor of gross anatomy, attended the Viking Fund dinner on Feb. 10 at the Waldorf Astoria Hotel in New York, when medals and awards for outstanding contributions in the field of anthropology for 1949 were presented.

Mr. Oliver Duggins, research assistant in anatomy, and Dr. Trotter attended a conference on growth, replacement and types of hair sponsored by the Section of Biology, New York Academy of Sciences in New York on Feb. 10-11. They presented a paper on "Changes in Morphology of Hair During Childhood." Dr. Trotter was chairman of one of the sessions.

Dr. Albert I. Lansing, assoicate professor of anatomy, at the invitation of the Los Angeles Tumor Institute, gave the first Albert Soiland Cancer Foundation lecture there on January 6. His topic was "The Significance of Calcium Binding Changes in Cancer and Ageing."

Bacteriology

Professor Wolfgang J. Henry of the Robert Koch Institute of Berlin visited the Department of Bacteriology here the week of April 3 to 11. He was traveling under auspices of the United States Public Health Service to visit bacteriology departments in several U. S. schools.

Internal Medicine

Dr. Samuel C. Bukantz, assistant dean and assistant professor of medicine, has been appointed to survey the needs and to act as administrator for the procurement and distribution of cortisone for investigative purposes in the School of Medicine. Merck and Company of Rahway, N. J., has made available a liberal supply of cortisone.

Dr. Henry A. Schroeder, associate professor of medicine, was guest speaker at the annual Alpha Omega Alpha lecture at St. Louis University on March 23. His topic was "The Pathology of Arterial Hypertension."

"The Relation of the Kidney to Acute Pressor Action of Desoxycorticosterone" was the subject of a paper presented by staff members at the Southern Society for Clinical Research, which met in New Orleans on March 17-18. The paper was prepared by Drs. Melvin L. Goldman, Henry A. Schroeder, Dean F. Davies, Joseph P. Kriss and Palmer H. Futcher. Drs. Kriss and Futcher are former members of the Department of Medicine.

Neuropsychiatry

Meetings of the American Orthopsychiatric Association in Atlantic City from Feb. 22 to 24 were attended by five members of the Department of Neuropsychiatry: Drs. George Saslow,

Samuel R. Warson, Robert I. Watson, James Palmer, and Margaret C.-L. Gildea. Dr. Saslow discussed a paper by Dr. A. I. Hallowell on "Cultural Values as a Factor in Behavior Disorder." A paper on "Family Structure and Psychic Development," co-authored by Dr. Warson and Dr. Jules Henry of the Department of Anthropology at the University, also was given. Dr. Henry organized this symposium.

Dr. Ivan Mensh, Dr. George Ulett, Dr. Sidney Goldring, Dr. Samuel R. Warson, and Mrs. Janet Golden attended a joint meeting of the Mid-Continent Psychiatric Association and the Missouri Society for Neurology and Psychiatry in Kansas City on March 18. Dr. Mensh and Mrs. Golden spoke on "Factors in Psychotherapeutic Success"; Drs. Ulett and Goldring on "DC Potentials Following Electro-Shock"; and Dr. Warson on "Child Psychiatry and Child Guidance."

Two German psychiatrists visited the department during the week of April 3 under the auspices of the United States Public Health Service. They were Dr. Heinrich Schulte, director of the Nervene Clinic in Bremen, and Dr. Gerde Ludwig, chief physician of Heilstetten Hospital in Berlin.

Obstetrics-Gynecology

After 43 years of private practice, Dr. Grandison D. Royston, associate professor of clinical ob.-gyn., retired from his Medical School position and his practice on March 1. He was honored at a testimonial dinner on that date, at which time Dr. Edward Schumann, Philadelphia gynecologist; Dr. Buford Hamilton, director of the Missouri State Health Division, and Dr. Robert A. Moore, Dean, praised his service to patients and students. Dr. Royston, a 1907 graduate of the Medical School, has retired to his farm near Hope, Ark.

Ophthalmology

Dr. Richard Scobee, assistant professor of ophthalmology, gave three lectures for the Florida Mid-Winter Seminar given from Jan. 15 to 18 in Miami Beach.

Dr. Lawrence T. Post, professor of clinical ophthalmology, toured veterans hospitals in the Sixth Area of the Veterans Administration during February. As consultant in ophthalmology for the area, he visited 11 hospitals in Missouri, Arkansas, Oklahoma and Texas.

Otolaryngology

Members of the Kansas City Otolaryngological and Ophthalmological Society visited the Departments of Otolaryngology and Ophthalmology on March 23. The departments presented lectures and case examples, with Drs. Theodore E. Walsh, G. O'Neil Proud, Joseph Ogura, Ben H. Senturia, Lawrence T. Post, Theodore Sanders, Paul W. Miles, and Richard G. Scobee, participating.

Pathology

Members of the Department attending the American Association of Pathologists and Bateriologists in Madison, Wis., on April 14-15 were: Drs. Robert A. Moore, Gustave Dammin, Margaret Smith, Frank J. Dixon, Thomas Young, Margaret Carter, William Snoddy, Cal-

vin J. Wegner, Raymond F. Hain, Humberto Torlini, Pradit Tansurat, Zola Cooper, and Lt. Col. Vernon D. Pettit.

Dr. Lauren V. Ackerman, associate professor of pathology and surgical pathology, gave two talks on cancer of the breast during March. Early in the month he spoke to the Central Surgical Society in Chicago, and on the 26th, to the College of American Pathologists, at St. Louis University.

Pediatrics

Pediatrics is now introduced to the sophomore class in the Medical School with a series of ten lectures which are a part of the course in medicine on applied pathological physiology.

Dr. Gilbert B. Forbes participated in the pediatrics postgraduate course at Baylor University College of Medicine in Houston, April 17-22. He lectured on trachael bronchitis and bronchiolitis, management of neo-natal infections, use of radioactive isotopes in pediatrics, and parenteral fluid therapy.

A nursery for premature infants was officially opened at St. Louis Children's Hospital on March 4, when the first patient was admitted. The nursery is a part of the Missouri Division of Health program for care of premature infants.

A $2,000,000 campaign for funds to build an addition to St. Louis Children's Hospital was officially opened on April 3. Dr. Alexis F. Hartmann, physician-in-chief, reports that the hospital is serving 35,000 children annually in the pediatrics outpatient department, and the need for additional space is acute. The growth has been so great in recent years that one out of three new patients now admitted to the Washington University Clinics is a child.

Radiology

A series of nine weekly lectures on radiation physics by Mr. F. W. Spiers, physicist to the Radiotherapy Centre at Leeds, England, was given from January 11 through March 8. The lectures were given on Wednesday evenings in Elliot Auditorium under sponsorship of the department of radiology. Mr. Spiers' topics were: physics in radiotherapy, physics in diagnostic radiology, physics in general medicine, organization of a medical physics department, and education in physics.

Drs. Otto Grunow, instructor, and Wayne Simril, assistant, were guest speakers at a meeting of the Illinois Chapter, College of Chest Physicians, in Chicago on February 10. Dr. Grunow's topic was "The Use of Sectional Radiology in Pulmonary and Mediastinal Disorders," and Dr. Simril's, "Cardiovascular Angiography with the Rapidograph."

Surgery

Drs. Evarts A. Graham and Thomas H. Burford attended the American Association for Thoracic Surgery meeting in Denver and the American Surgical Association in Colorado Springs during April. Alumni members of the American Board met in Denver also. Dr. Graham was president of the original group which was organized here.

Dr. Robert Elman addressed the Denver General Hospital Medical and Surgical Society on January 12, speaking on "The Indication for and Methods of Intravenous Alimentation."

Publications of the Faculty

January - March, 1950

Allen, W. M. A simple method for analyzing complicated absorption curves, of use in the colorimetric determination of urinary steroids. J. clin. endocrinol. *10:* 71-83. Jan., 1950.

Allen, W. M., Hayward, S. J., and Pinto, A. A color test for dehydroisoandrosterone and closely related steroids, of use in the diagnosis of adreno-cortical tumors. J. clin. endocrinol. *10:* 54-70. Jan., 1950.

Alexander, H. L., Glaser, R. J., and Harford, C. G. Respiratory infection, arthralgia and renal failure. Clinio-pathologic conference. Am. j. med. *8:* 229-238. Feb., 1950.

Alexander, H. L., Hunter, T. H., and Goldman, A. Skin eruption, obtundity and pyrexia. Clinico-pathologic conference. Am. j. med. *8:* 384-392. March, 1950.

Bartlett, R. W. The surgical management of large goiters. Postgrad. med. *7:* 58-62. Jan., 1950.

Blair, V. P., and Letterman, G. S. The role of the switched lower lip flap in upper lip restorations. Plastic and reconstructive surgery *5:* 1-25, January, 1950.

Black, H. Fibrosarcoma of the bronchus. Jl. thor. surg. *19:* 123-134. Jan., 1950.

Brown, J. B., and Byars, L. T. The treatment of burns. Brennemann's practice of pediatrics. V. 4, chap. 42, p. 1-13.

Brown, J. B., McDowell, F., and Fryer, M. P. Direct operative removal of benign mixed tumors of anlage origin in the parotid region. With summary of parotid tumors in general. Surg., gynec., and obst. V. 90, March, 1950, p. 257-268.

Burford, T. H., Carson, M. J., and Scott, W. G. Angiocardiography and aortography in the diagnosis of congenital cardiovascular lesions. J. thor. surg. *18:* 860-868, December, 1949.

Byars, L. T. Cancer of the face, mouth and neck; principles of surgical treatment. J. Missouri state med. assn. *47:* 169-172. March, 1950.

Byars, L. T., and DeMere, McC. Restoration of the missing ear. Plastic and reconstructive surgery *5:* 66-74. Jan., 1950.

Charles, C. M. Treatment of hereditary cephalagia. Postgrad. med. *7:* 33-35. Jan., 1950.

Chieffi, M. An investigation of the effects of parenteral and topical administration of steroids on the elastic properties of senile skin. J. gerontol. *5:* 17-22. Jan., 1950.

Chieffi, M. Gerontology: science of complex problems. Hosp. progress *31:* 48-49. Feb., 1950.

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Drake, T. G. Agranulocytosis during therapy with the antihistaminic agent methaphenilene (Diatrin). J. Am. med. assn. *142:* 477-478. February 18, 1950.

Eckert, Charles, and Ackerman, L. V., eds. Tumor conference. Washington university school of medicine. Jl. Missouri state med. assn. *47:* 119-125. Feb., 1950.

Forbes, G. B., Deisher, R. W., Perley, A. M., and Hartmann, A. F. Effect of hyaluronidase on the subcutaneous absorption of electrolytes in humans. Science *111:* 177-179. Feb. 17, 1950.

Futcher, P. H., and Massie, E. Agranulocytosis due to propylthiouracil. Ann. int. med. *32:* 137-138. Jan., 1950.

Gest, H., Kamen, M. D., and Bregoff, H. M. Studies on the metabolism of photosynthetic bacteria. V. Photoproduction of hydrogen and nitrogen fixation by Rhodospirillum rubrum. Jl. biol. chem. *182:* 153-170, Jan., 1950.

Gildea, E. F. Special features of personality which are common to certain psychosomatic disorders. Psychosomat. med. *11:* 273-281. Sept.-Oct., 1949.

Graham, E. A. Changing concepts in surgery. Postgrad. med. *7:* 154-156. Feb., 1950

Graham, E. A. Diagnosis and treatment of pulmonary suppuration. Postgrad. med. *7:* 202-205. March, 1950.

Granick, S. Studies in the psychology of senility—a survey. J. gerontol. *5:* 44-58. Jan., 1950.

Grinstein, M., Kamen, M. D., Wikoff, H. M., and Moore, C. V., Isotopic studies of porphyrin and hemoglobin metabolism. I. Biosynthesis of coproporphyrin I and its relationship to hemoglobin metabolism. J. biol. chem. *182:* 715-721. February, 1950.

Harford, C. G., and Hara, M. Pulmonary edema in influenzal pneumonia of the mouse and the relation of fluid in the lung to the inception of pneumococcal pneumonia. J. exp. med. *91:* 245-261. March, 1950.

Hartmann, A. F. Acidosis and alkalosis. Brennemann's practice of pediatrics. V. 1, chap. 24, p. 1-19.
Key, J. A. Intervertebral-disc lesions in children and adolescents. J. bone and joint surg. *32-A:* 97-102. Jan., 1950.
Kvorning, S. A. The silica content of the aortic wall in various age groups. J. gerontol. *5:* 23-25. Jan., 1950.
Liang, H. M. Localized changes in methylcholanthrene treated epidermis. Acta unio internationalis cancrum *6:* 733-735. 1949.
Marcus, M. D., and Frerichs, J. B. Dermatitis due to contact with iodoacetic acid. J. Am. med. assn. *142:* 805-806. March 18, 1950.
Marcus, M. D., and Wooldridge, W. E. Sebaceous nevus and nevus syringoadenomatosus papilliferus occurring as a mixed form. Arch. dermat. and syphil. *61:* 105-108. Jan., 1950.
Maughs, S. B. Phychopathic personality. Review of the literature, 1940-47. J. clin. psychopath. *10:* 247-275, July, 1949.
McCarroll, H. R. Trials and tribulations in attempted femoral lengthening. J. bone and joint surg. *32-A:* 132-142. Jan., 1950.
Mead, S. Physical medicine in general practice. Postgrad. med. *7:* 54-57. Jan., 1950.
Proetz, A. W. Natural defenses and disorders of the respiratory tract. Trans. med. soc. of London. *65:* 498-504. 1947-49.
Reinhard, E. H., Good, J. T., and Martin, E. Chemotherapy of malignant neoplastic diseases. J. Am. med. assn. *142:* 383-390. Feb. 11, 1950.
Roos, A., and Black, H. Direct determination of partial and total tensions of respiratory gases in blood. Am. j. physiol. *160:* 163-176. Jan. 1, 1950.
Rosenschweig, S. Levels of behavior in psychodiagnosis with special reference to the picture-frustration study. Am. j. orthopsychiat. *20:* 63-72. Jan., 1950.
Ruangsiri, Chanai. Changes in islets of Langerhans in living mice after alloxan administration. Anat. rec. *105:* 399-427. Nov., 1949.
Scott, V. Hyaluronidase and experimental syphilis. II. The attempted localization of lesions in syphilitic rabbits by intradermal and by intracorneal injections of hyaluronidase. A negative report. Am. jl. syphilis *34:* 12-17, January, 1950.
Scott, V., and Droegemueller, C. Hyaluronidase and experimental syphilis. I. The length of incubation periods in experimental primary syphilis with and without hyaluronidase. Am. jl. syphilis *34:* 1-11, January, 1950.
Silberberg, M., and Silberberg, R. Malignant lymphoid tumors in orchidectomized mice receiving hypophyseal and ovarian grafts at various ages. Proc. soc. exp. biol. and med. *72:* 547-550. Dec., 1949.
Silberberg, R., and Silberberg, M. Skeletal growth and articular changes in mice receiving a high-fat diet. Am. jl. path. *26:* 113-131. Jan., 1950.
Starkloff, G. B., Bricker, E. M., McDonald, J. J., and Litzow, L. T. Proximal femoral venography; a preliminary report. Ann. surg. *131:* 413-417. March, 1950.
Stock, C. C., and Schroeder, H. A. Pressor substances in arterial hypertension: activity and amine content of crude extracts of blood. Am. j. physiol. *160:* 409-420. Feb., 1950.
Thale, T., Gabrio, B. W., and Salomon, K. Hallucination and imagery induced by mescaline. Am. j. psychiatry *106:* 686-691. March, 1950.
Woo, J.-K. Ossification and growth of the human maxilla, premaxilla and palate bone. Anat. rec. *105:* 737-753. Dec., 1949.
Wood, W. B., Jr. The limits of biomorphology. (Editorial.) Am. j. med. *8:* 137-138. Feb., 1950.
Wood, W. B., Jr., Grunow, O. H. W., and Taussig, B. L. Hematuria, pneumonia, and cachexia. Clinico-pathologic conference. Am. jl. med. *8:* 106-114. Jan., 1950.
Wood, W. B., Jr., and Smith, M. R. The nature and biological significance of the capsular slime layer of pneumococcus type III. Trans. Assn. Am. Physn. *62:* 90-92. 1949.
Wren, C., and Sachar, L. Amount of carbohydrate required to prevent ketonuria in patients after operation. Surg., gynec., and obst. V. 90, March, 1950, p. 349-352.

Copies of October '47 Quarterly Wanted

If you have a spare copy of the October, 1947, issue of the *Medical Alumni Quarterly* (Volume XI, Number 1), the Medical School Library would appreciate receiving it.

Alumni News

1901

Walter C. G. Kirchner and **Joseph Grindon, Sr.,** '79, received the first merit awards of the St. Louis City Hospital Alumni Association at the 62nd dinner meeting of the group on March 29. The awards are given for service to the hospital. Dr. Grindon, who died April 1, and Dr. Kirchner have been members of the association for more than 50 years. Dr. Grindon was on the house staff in 1879-80, and Dr. Kirchner in 1901-02. Both have been members of the visiting staff ever since.

1891

J. W. Craig has offices at the Security Building in Miami, Okla.

P. H. Morrison moved recently to 4915 Lindell Blvd., St. Louis.

1896

Meyer Wiener, who is professor emeritus of clinical ophthalmology in the Medical School, is living at 321 Alameda Blvd., Box 516, Coronado, Calif. His recent activities include a course on "Surgery of Lid Paralysis" at the Mid-Winter Postgraduate Assembly of the Research Study Club in Los Angeles on January 16. During February he addressed a joint meeting of the Pensacola Medical Society and the Aviation School of Medicine at Pensacola, Fla. In March he was guest speaker for the Georgia State Medical Society in Savannah, and for the New York Society of Clinical Ophthalmology. Dr. Wiener retired in July, 1946, from his W. U. position.

1899

C. L. Lawless is living in Marshall, Mo.

1910

Robert M. Hardaway, who is retired Brigadier General in the U. S. Army, lives at 4052 Field Drive, Wheatridge, Colo.

1911

John F. Barton's new address is 1609 21st Ave., in Longview, Wash.

William Edler now lives at 1230 Glen Oaks, Pasadena, Calif.

1914

John T. McLarney can be reached at 1002 N. Main St., in Brookfield, Mo.

1920

Adolph S. Rumreich recently was appointed Public Health Service Regional Medical Director for Federal Security Agency Region 5, with headquarters in Chicago. He was commissioned in the Regular Corps of the Public Health Service in 1924, and has been in the Chicago office since 1941, directing activities in connection with the Hospital Facilities program. He holds a doctor of public health degree from Johns Hopkins School of Hygiene and Public Health.

1922

James B. Costen, associate professor of clinical otolaryngology in the Medical School, addressed the Ear, Nose and Throat Club of New Orleans March 1, on tumors of the larynx.

Leon G. Campbell recently moved to 960 E. Green St., Pasadena, Calif.

1923

John W. Williams, Jr., recently moved from Jefferson City to 1227 Roanoke, Springfield, Mo.

Ben D. Senturia has an office at 1031 W. North Shore Avenue in Chicago, Ill.

George H. Klinkerfuss is in general practice at 340 Bermuda Avenue, Normandy, Mo.

1924

Perry E. Duncan's address is 405 E. Capitol Ave., Springfield, Ill.

Capt. Dwight J. Wharton is commanding officer at the U. S. Naval Hospital in Jacksonville, Fla.

1925

Abraham E. Hiebert's address is 1530 Parker, Wichita, Kan.

1926

Ralph Berg recently moved to 5044 Potomac in St. Louis.

1927

Irene A. Koeneke is associated with the Hertzler Clinic in Halstead, Kan., specializing in surgery.

Alfred J. Metscher writes from Enid, Okla., that other W. U. medical men there are **George Wilson** '27, **William P. Neilson** '27, **Paul Champlin** '20, and **James G. Tagge,** '42.

1928

Frank R. Bradley, director of Barnes Hospital, spoke to the American Protestant Hospital Association in Chicago, March 3, on "Peering into the Future—Who Will Control Our Hospitals?"

Justin J. Cordonnier, assistant professor of clinical genitourinary surgery, presented a movie on ureteral sigmoid anastomosis before the American Urological Association at Biloxi, Miss., on February 1.

Charles L. Caldwell can be reached at 115 E. 18th St., Tulsa, Okla.

Laurence L. Howard lives at 711 Fourth Ave., No., Great Falls, Mont.

George H. Wood is practicing in Carthage, Mo.

1929

William P. Shelton is now in Dallas, Tex., at 2600 Welborn St., and specializing in neurology and psychiatry with Clarence S. Hoekstra, M.D.

1930

James P. Conway is practicing pediatrics at 1721 E. Lake Bluff Blvd. in Milwaukee, Wis.

Harold S. Bowman has an office at 205 K.F.H. Bldg., Wichita, Kan.

1932

Dwight H. Trowbridge is located in the T. W. Patterson Bldg., Fresno, Calif.

1934

Ralph C. Greene is at the Veterans Administration Center in Martinsburg, W. Va.

1935

Norman M. Johnson is in Clarinda, Iowa.

1937

William J. Quinn is practicing in Alturas, Modoc County, Calif.

Samuel M. Day recently moved his offices to the Professional Bldg., in Jacksonville, Fla.

H. C. Gehrand has moved to 960 E. Green St., Pasadena, Calif.

1938

Robert G. Moles is practicing in Hartford, Calif.

Harry E. Mantz is in the Elfgen Bldg., Alton, Ill.

1939

Robert E. Shank, professor of preventive medicine in the Medical School, recently was appointed to the Committee of Research and Standards of the Missouri Public Health Association.

Joseph Borenstine's address is 121 W. 63rd St., Kansas City, Mo.

A. Waite Bohne is at University Hospital of Ohio State University, Columbus, Ohio.

Mark Brockbank can be reached at 408 Melvin in Petaluma, Calif.

Judson D. Dowling and **Luther Davis** '34 are associated in practice at 2507 Sixth Street in Tuscaloosa, Ala. Dr. Dowling recently moved there from Mt. Olive, N. C. He is married and the father of five boys.

Frank L. Davis, Jr., recently announced the opening of his office in the University Club Building in St. Louis, with practice limited to general surgery.

1941

V. A. Mueller's office is in the Schweits Bldg., Wichita, Kan.

R. Wendell Stewart has moved to 2408 Windsor Dr., Springfield, Mo.

1942

Souther F. Tompkins is in the Medical Arts Bldg. at Oklahoma City, Okla. He recently moved there from Rochester, Minn.

Warren B. Mills lives at 445 Fairview Ave., Webster Groves, Mo.

1943

Herbert C. Wiegand lives at 840 Oakbrook Lane, University City, Mo.

James G. Owen is connected with the Virginia Mason Clinic in Seattle, Wash.

John F. Blinn, Jr., can be reached at 1413 Argonne Dr., Stockton, Calif.

Joseph B. Clay recently opened his offices for the practice of internal medicine at 14544 Gilmore St., Van Nuys, Calif.

Walter A. Rohlfing, Jr., is medical director of the General Hospital of Fresno County, Fresno, Calif.

John L. Crites has moved to 307 26th St., Charleston, W. Va.

1944

Francis E. Pennington can be reached at Box 295, Route 5, Kirkwood, Mo.

Ervan Levine has just opened offices for practice in Vandalia, Mo.

1945

William H. Crouch, Jr., is practicing in Macon, Mo.

Gary B. Wood lives at 433 Woodlawn in Webster Groves, Mo.

Ceylon S. Lewis, Jr., is at 1815 E. 9th St., South, Salt Lake City, Utah.

Clarence E. Rupe has moved to 1750 E. Grand Blvd., Detroit, Mich.

Thomas J. Fitzpatrick writes that he has enjoyed receiving the QUARTERLY, and that his new address is 4265 Cleveland Ave., in St. Louis.

John P. Roberts can be reached in care of the Museum of Transport, Barrett Station Road, Kirkwood, Mo.

1946

Robert E. Lee's address is 278 Steele, in Denver, Colo.

Joseph C. Williams' new address is 1025 Greenway Terrace, Kansas City, Mo.

1947

Robert T. Polack is with the Michigan State Sanatorium in Howell, Mich.

1948

David A. Guterman wrote recently that he finished his internship at Jewish Hospital in St. Louis in June, 1949. Since July, 1949, he has been serving as first year psychiatric resident at Elgin State Hospital in Elgin, Ill.

In Memoriam

1879

Dr. Joseph Grindon, Sr., died of infirmities at St. Mary's Hospital in St. Louis on April 1. Dr. Grindon was 91 years old, and his 66 years as a practicing physician in St. Louis covered a period which saw the city develop into a leading medical center. He was professor emeritus of dermatology at St. Louis University Medical School at the time of his death. When he retired from active duties in 1944, he was the oldest practicing physician in St. Louis. During his career he had served on the staffs of most of the hospitals in the city, and was dermatologist-in-chief at St. Mary's Hospital from 1924 to 1944. In 1929, he was honored by the St. Louis University and Washington University Schools of Medicine, with the St. Louis Medical Society also participating, on the occasion of his 50th anniversary of graduation. He was a former president of the St. Louis Medical Society and of the local and national dermatological organizations. St. Louis University awarded him the honorary degree of doctor of science in 1943. Surviving are his son, Dr. Joseph Grindon, Jr., and two daughters. Mrs. Grindon died in 1935.

1882

Notice has been received of the death of **Luther Longino** of Minden, La.

1894

J. D. Brazeel died November 26, 1949, in Okemah, Okla.

1898

J. G. Massie, who lived at 121a East Main St., Belleville, Ill., died recently.

1899

Joseph C. Weber of Olney, Ill., died in May, 1949.

1891

Walter E. Gibson died recently at his home in De Soto, Mo.

1904

Cleo C. Ball of Ravenden, Ark., died November 4, 1949.

D. B. Garstang of Los Angeles, Calif., died on March 6, 1950, at the age of 70. He had been on the staff of Queen of Angels Hospital there since it opened in 1928. Dr. Garstang, a urologist, was a former president of the Washington University Los Angeles chapter of the Alumni Association.

1913

W. E. Koppenbrink died suddenly of coronary thrombosis on March 1, 1950, at his home in Higginsville, Mo., at 59 years of age. He had served internships at Barnes and Children's Hospitals, and a residency at St. Luke's Hospital in St. Louis. He had been president, secretary and treasurer of the Lafayette County Medical Society, and had been county coroner and physician at the Confederate Home of Missouri, and chairman of the City Board of Health. Dr. Koppenbrink was a member of the Missouri State and Southern Medical Associations; a Fellow of the A. M. A.; and a member of Phi Beta Pi. He served as first lieutenant in the Medical Corps during World War I. At the time of his death he was county physician and was associated with his son, Walter E. Koppenbrink, Jr., M.D., in practice.

1936

Arthur C. Darrow died suddenly February 16, 1950, in San Fernando, Calif., where his home was at 14249 Tyler Rd.

WASHINGTON UNIVERSITY

Arthur H. Compton, Ph.D., Sc.D., LL.D., *Bridge Chancellor*
Charles Belknap, B.S., *Vice-Chancellor*

Edward K. Graham, Ph.D., *Dean of Faculties*

Thomas E. Blackwell, Ph.B., M.S., J.D.,
Director of Business Administration

The College of Liberal Arts
Thomas S. Hall, Ph.D., Dean

The School of Engineering
Lawrence E. Stout, Ph.D., Ch.E., Dean

The School of Architecture
Joseph D. Murphy, Dean

The School of Business and Public Administration
Leslie J. Buchan, Ph.D., Dean

The George Warren Brown School of Social Work
Benjamin E. Youngdahl, A.M., Dean

The Henry Shaw School of Botany
Henry N. Andrews, Jr., Ph.D., Acting Dean

The Graduate School of Arts and Sciences
Carl Tolman, Ph.D., Dean

The School of Law
Wayne L. Townsend, A.B., LL.B., J.S.D., Dean

The School of Medicine
Robert A. Moore, M.D., Ph.D., Dean

The School of Dentistry
Otto W. Brandhorst, D.D.S., Dean

The School of Nursing
Louise Knapp, R.N., B.S., A.M., Director

The School of Fine Arts
Kenneth E. Hudson, B.F.A., Dean

University College
Willis H. Reals, Ph.D., Dean

The Summer School
Frank L. Wright, A.M., Ed.D., Director

The Henry Edwin Sever Institute of Technology
Lawrence E. Stout, Ph.D., Ch.E., Director